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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:42:24 ON 06 JUN 2007

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 08:42:34 ON 06 JUN 2007
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 5 JUN 2007 HIGHEST RN 936615-27-9
DICTIONARY FILE UPDATES: 5 JUN 2007 HIGHEST RN 936615-27-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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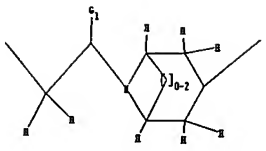
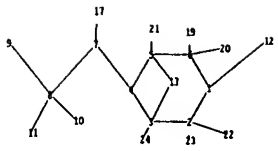
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10539106.str





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7 8 9 10 11 12 17 19 20 21 22 23 24
ring nodes :
1 2 3 4 5 6 13
chain bonds :
1-12 2-22 2-23 3-24 4-7 5-21 6-19 6-20 7-8 7-17 8-9 8-10 8-11
ring bonds :
1-2 1-6 2-3 3-4 3-13 4-5 5-6 5-13
exact/norm bonds :
1-2 1-6 2-3 3-4 3-13 4-5 4-7 5-6 5-13 7-17
exact bonds :
1-12 2-22 2-23 3-24 5-21 6-19 6-20 7-8 8-9 8-10 8-11
isolated ring systems :
containing 1 :

G1:C,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:Atom 17:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS
23:CLASS 24:CLASS

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L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1                STR
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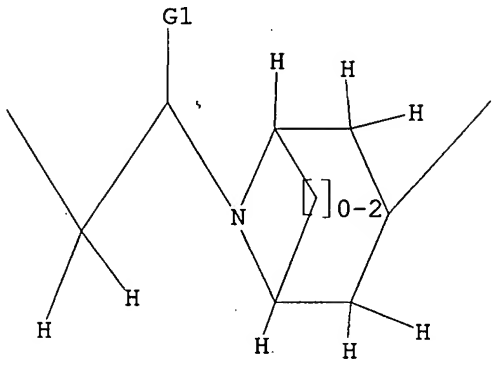


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G1 C,H


Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 08:43:05 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      196 TO ITERATE

100.0% PROCESSED      196 ITERATIONS                                  4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         3081 TO     4759
PROJECTED ANSWERS:               4 TO      200

L2             4 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 08:43:09 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     3815 TO ITERATE

100.0% PROCESSED     3815 ITERATIONS                               133 ANSWERS
SEARCH TIME: 00.00.01

L3           133 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   172.10     172.31

FILE 'CAPLUS' ENTERED AT 08:43:13 ON 06 JUN 2007
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FILE COVERS 1907 - 6 Jun 2007 VOL 146 ISS 24
FILE LAST UPDATED: 5 Jun 2007 (20070605/ED)

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http://www.cas.org/infopolicy.html

=> s l3 full
L4 28 L3

=> d ibib abs hitstr tot

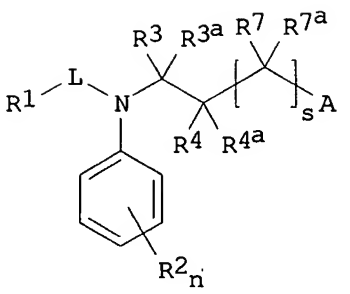
L4 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1285816 CAPLUS
DOCUMENT NUMBER: 146:45547
TITLE: Preparation of aryl bicyclo and spiro compounds as therapeutic modulators of CCR-5 activity
INVENTOR(S): Boman, Erik; Dahl, Russell; Delaet, Nancy G. J.; Ernst, Justin; Lum, Christopher; Sebo, Lubomir; Urban, Jan
PATENT ASSIGNEE(S): Kemia, Inc., USA
SOURCE: PCT Int. Appl., 235pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006130426 | A2 | 20061207 | WO 2006-US20255 | 20060525 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-685147P P 20050527
US 2006-785090P P 20060322

OTHER SOURCE(S): MARPAT 146:45547
GI



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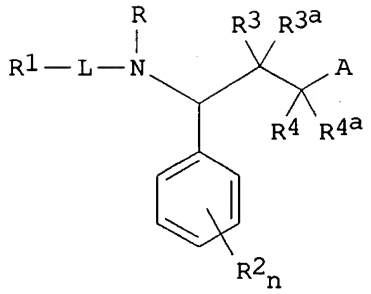
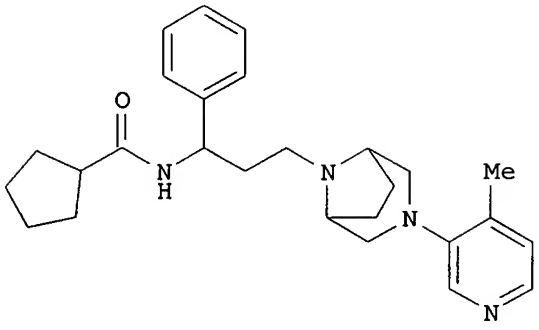


II



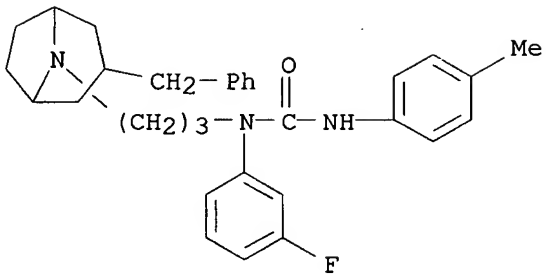
III

AB The present invention relates to low mol. weight compds., including compds. of Formulas I and II, and pharmaceutical compns. thereof, useful as modulators of CCR-5 activity (no biol. activity given). For I and II, A = a substituted spiro, bicyclo, or piperazinyl ring; R1 = (un)substituted alkyl, alkenyl, alkynyl, aryl, aralkyl, heterocyclyl or heterocyclylalkyl group; R2= halo or (un)substituted C1-C4 alkyl; R3, R3a, R4, R4a, R7, and R7a = H, halo, or (un)substituted C1-6 alkyl or C1-4 alkoxy group; and n = 0-5. The invention further relates to the use of such compds. and compns. in treating disorders mediated by CCR-5 such as viral infections and inflammatory diseases. Preparation methods for I and II are disclosed. For example, III is prepared by reacting 8-boc-3,8-diaza-3-(4-methylpyrid-3-yl)bicyclo[3.2.1]octane (preparation given) and (S)-tert-Bu 3-oxo-1-phenylpropylcarbamate to give an amine intermediate which is subsequently reacted with cyclopentyl carbonyl chloride.

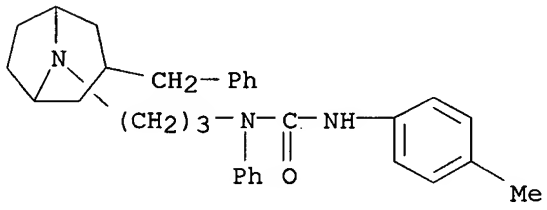
IT 916454-94-9P 916454-95-0P 916454-96-1P
916454-97-2P 916458-71-4P, 1-Acetyl-N-[3-(3-benzyl-8-azabicyclo[3.2.1]octan-8-yl)propyl]-N-phenylpiperidine-4-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aryl bicyclo and spiro compds. as therapeutic modulators of CCR-5 activity)

RN 916454-94-9 CAPLUS

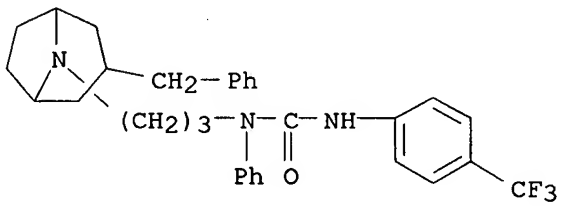
CN Urea, N-(3-fluorophenyl)-N'-(4-methylphenyl)-N-[3-[3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (CA INDEX NAME)



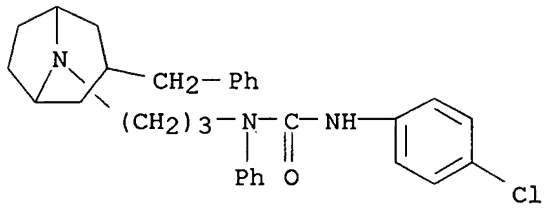
RN 916454-95-0 CAPLUS
CN Urea, N'-(4-methylphenyl)-N-phenyl-N-[3-[3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (CA INDEX NAME)



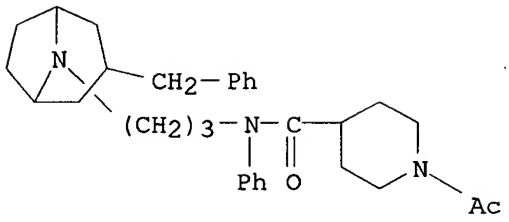
RN 916454-96-1 CAPLUS
CN Urea, N-phenyl-N-[3-[3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]-N'-[4-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 916454-97-2 CAPLUS
CN Urea, N'-(4-chlorophenyl)-N-phenyl-N-[3-[3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (CA INDEX NAME)

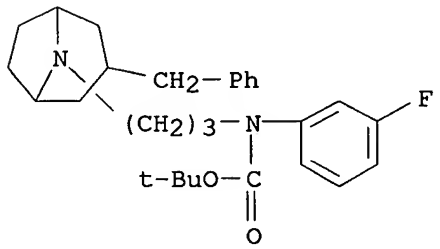


RN 916458-71-4 CAPLUS
CN 4-Piperidinecarboxamide, 1-acetyl-N-phenyl-N-[3-[3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (CA INDEX NAME)

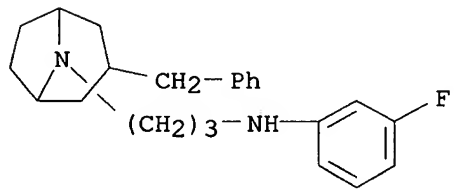


IT 916458-67-8P, tert-Butyl N-[3-(3-benzyl-8-azabicyclo[3.2.1]octan-8-yl)propyl](3-fluorophenyl)carbamate 916458-68-9P, N-[3-(3-Benzyl-8-azabicyclo[3.2.1]octan-8-yl)propyl]-3-fluoroaniline 916458-69-0P, tert-Butyl N-[3-(3-benzyl-8-azabicyclo[3.2.1]octan-8-yl)propyl](phenyl)carbamate 916458-70-3P, N-[3-(3-Benzyl-8-azabicyclo[3.2.1]octan-8-yl)propyl]aniline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aryl bicyclo and spiro compds. as therapeutic modulators of CCR-5 activity)

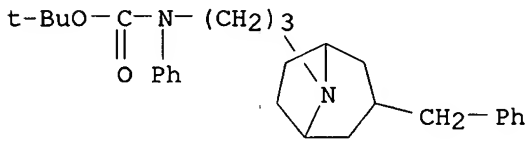
RN 916458-67-8 CAPLUS
CN Carbamic acid, N-(3-fluorophenyl)-N-[3-[3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



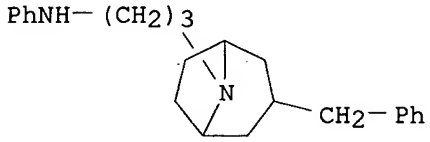
RN 916458-68-9 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-8-propanamine, N-(3-fluorophenyl)-3-(phenylmethyl)- (CA INDEX NAME)



RN 916458-69-0 CAPLUS
CN Carbamic acid, N-phenyl-N-[3-[3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 916458-70-3 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-8-propanamine, N-phenyl-3-(phenylmethyl)- (CA INDEX NAME)



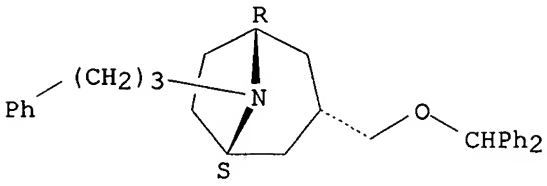
L4 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1108680 CAPLUS
DOCUMENT NUMBER: 146:19364
TITLE: Synthesis of dopamine transporter selective 3-diarylmethoxymethyl-8-arylalkyl-8-azabicyclo[3.2.1]octane derivatives
AUTHOR(S): Zhang, Suhong; Izenwasser, Sari; Wade, Dean; Xu, Liang; Trudell, Mark L.
CORPORATE SOURCE: Department of Chemistry, University of New Orleans, USA
SOURCE: Bioorganic & Medicinal Chemistry (2006), 14(23), 7943-7952
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:19364
AB A series of diarylmethoxymethyltropane-GBR hybrid analogs with all three possible stereochem. orientations at C3 were synthesized and evaluated at dopamine and serotonin transporters. The 3α derivs. were found to be the most potent compds. with the 3α-di(4-fluorophenyl)methoxymethyl-8-(3-phenylpropyl)-8-azabicyclo[3.2.1]octane 15b (Ki = 5 nM) being the most potent compound of the series. The corresponding 3-di(4-fluorophenyl)-methoxymethyl-8-(3-phenylpropyl)-8-azabicyclo[3.2.1]oct-2-ene 12b (Ki = 12 nM) was slightly less potent than the 3α-analog, while the 3β-di(4-fluorophenyl)methoxymethyl-8-(3-phenylpropyl)-8-azabicyclo[3.2.1]octane 23b (Ki = 78 nM) exhibited only modest affinity for the dopamine transporter. Only the 3α-analog 15b (SERT/DAT = 48) exhibited higher SERT/DAT selectivity than GBR 12909. These results indicate that the dopamine transporter can tolerate some variability in proximity of the benzhydryl ether to the basic nitrogen atom of the tropane without loss in potency. In addition, the structure-activity data for these tropane-GBR 12909 hybrid analogs support previous findings that the stereochem. and conformational effects imparted by unsatn. at C3 are important for dopamine transporter selectivity over the serotonin transporter.
IT 915098-04-3P 915098-06-5P 915217-69-5P
915217-71-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dopamine transporter selective azabicyclooctane derivs.)
RN 915098-04-3 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[(diphenylmethoxy)methyl]-8-(3-phenylpropyl)-, (3-endo)-, ethanedioate (1:1) (CA INDEX NAME)

CM 1

CRN 915098-03-2

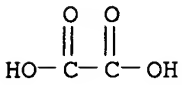
CMF C30 H35 N O

Relative stereochemistry.




CM 2

CRN 144-62-7
CMF C2 H2 O4




RN 915098-06-5 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[[bis(4-fluorophenyl)methoxy]methyl]-8-(3-phenylpropyl)-, (3-endo)-, ethanedioate (1:1) (CA INDEX NAME)

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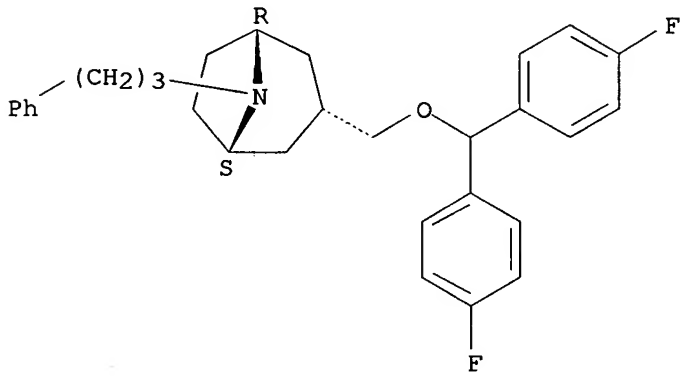
CRN 915098-05-4
CMF C30 H33 F2 N O

Relative stereochemistry.

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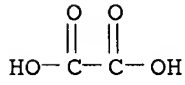


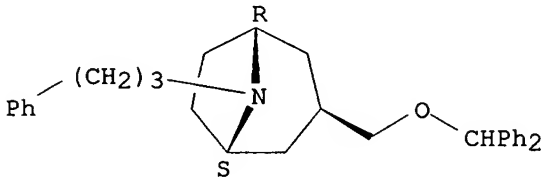

RN 915217-69-5 CAPLUS

CN 8-Azabicyclo[3.2.1]octane, 3-[(diphenylmethoxy)methyl]-8-(3-phenylpropyl)-, ethanedioate (1:1), (3-exo)- (CA INDEX NAME)

CM 1

CRN 915217-68-4
CMF C30 H35 N O

Relative stereochemistry.

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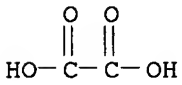
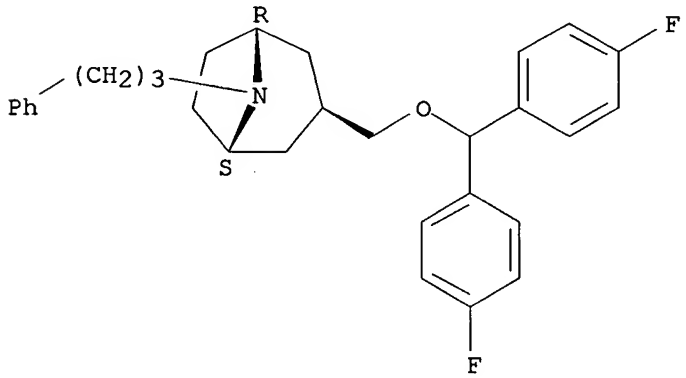



RN 915217-71-9 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[[bis(4-fluorophenyl)methoxy]methyl]-8-(3-phenylpropyl)-, ethanedioate (1:1), (3-exo)- (CA INDEX NAME)

CM 1

CRN 915217-70-8
CMF C30 H33 F2 N O

Relative stereochemistry.




CM 2

CRN 144-62-7
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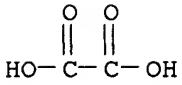
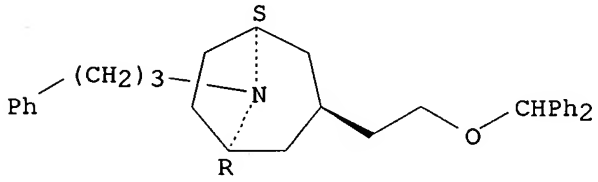


IT 548459-03-6 548459-05-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dopamine transporter selective azabicyclooctane derivs.)

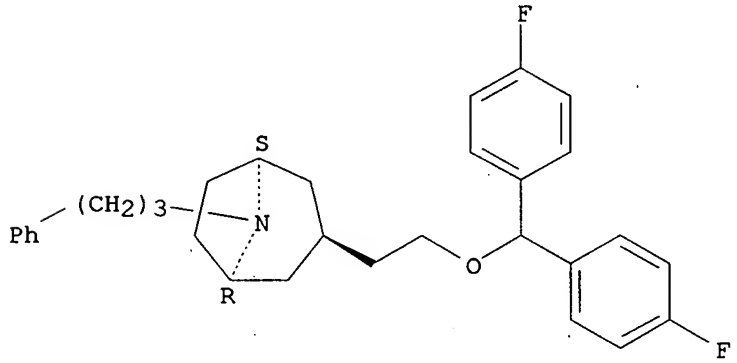
RN 548459-03-6 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[2-(diphenylmethoxy)ethyl]-8-(3-phenylpropyl)-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.



RN 548459-05-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[2-[bis(4-fluorophenyl)methoxy]ethyl]-8-(3-phenylpropyl)-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2005:451115 CAPLUS |
| DOCUMENT NUMBER: | 143:7605 |
| TITLE: | A preparation of azabicyclo[3.2.1]octane derivatives, useful as M3 muscarinic acetylcholine receptor antagonists |
| INVENTOR(S): | Wan, Zehong; Yan, Hongxing; Palovich, Michael R.; Laine, Dramane I.; Lee, Dennis; Stavenger, Robert A.; Goodman, Krista B.; Hilfiker, Mark A.; Cui, Haifeng; Viet, Andrew W.; Marino, Joseph P. |
| PATENT ASSIGNEE(S): | Glaxo Group Limited, UK |
| SOURCE: | PCT Int. Appl., 48 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 1 |

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005046586 | A2 | 20050526 | WO 2004-US36663 | 20041104 |
| WO 2005046586 | A3 | 20050728 | | |
| WO 2005046586 | A8 | 20050901 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1682142 | A2 | 20060726 | EP 2004-810294 | 20041104 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS | | | | |
| JP 2007510731 | T | 20070426 | JP 2006-539633 | 20041104 |
| PRIORITY APPLN. INFO.: | | | US 2003-517243P | P 20031104 |
| | | | WO 2004-US36663 | W 20041104 |

OTHER SOURCE(S): CASREACT 143:7605; MARPAT 143:7605
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

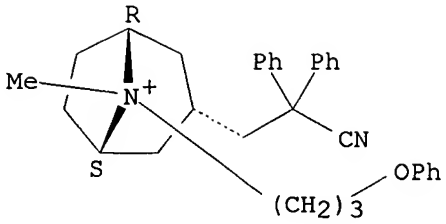
AB The invention relates to a preparation of azabicyclo[3.2.1]octane derivs. of formula I•X- [wherein: X- is an anion; R1 is alkyl, alkenyl, alkylcycloalkyl, or alkyl-OMe, etc.; R2 is (cyclo)alkyl, heterocycloalkyl, or cycloalkylalkyl, etc.], useful as M3 muscarinic acetylcholine receptor antagonists (no biol. data). For instance, quaternary azabicyclo[3.2.1]octane derivative II•Br- was prepared via quaternization of N-methylazabicyclo[3.2.1]octane derivative III by cyclopropylmethyl bromide with a yield of 51%.

IT 852436-02-3P 852460-99-2P 852461-00-8P
852461-03-1P 852461-04-2P 852461-05-3P
852461-10-0P 852461-12-2P 852461-18-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azabicyclo[3.2.1]octane derivs. useful as M3 muscarinic acetylcholine receptor antagonists)

RN 852436-02-3 CAPLUS

CN 8-Azoniabicyclo[3.2.1]octane, 3-(2-cyano-2,2-diphenylethyl)-8-methyl-8-(3-phenoxypropyl)-, bromide, (3-endo,8-syn)- (9CI) (CA INDEX NAME)

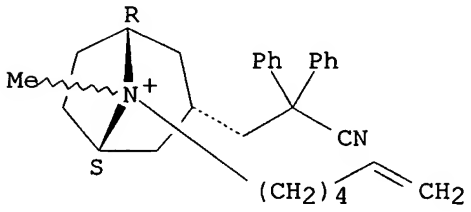
Relative stereochemistry.




● $Br^-$

RN 852460-99-2 CAPLUS
CN 8-Azoniabicyclo[3.2.1]octane, 3-(2-cyano-2,2-diphenylethyl)-8-(5-hexenyl)-8-methyl-, bromide, (3-endo,8-syn)- (9CI) (CA INDEX NAME)

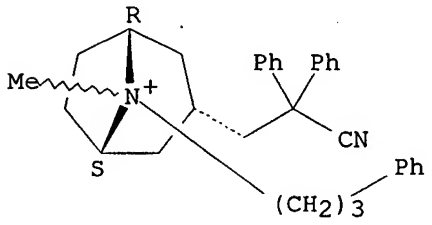
Relative stereochemistry.




● $Br^-$

RN 852461-00-8 CAPLUS
CN 8-Azoniabicyclo[3.2.1]octane, 3-(2-cyano-2,2-diphenylethyl)-8-methyl-8-(3-phenylpropyl)-, bromide, (3-endo,8-syn)- (9CI) (CA INDEX NAME)

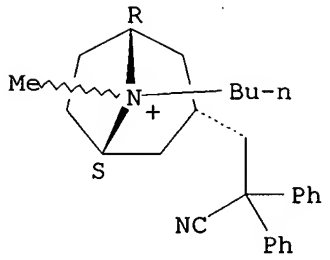
Relative stereochemistry.




● $Br^-$

RN 852461-03-1 CAPLUS
CN 8-Azoniabicyclo[3.2.1]octane, 8-butyl-3-(2-cyano-2,2-diphenylethyl)-8-methyl-, bromide, (3-endo,8-syn)- (9CI) (CA INDEX NAME)

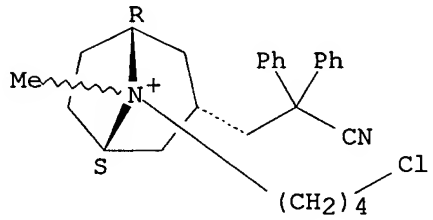
Relative stereochemistry.




● $Br^-$

RN 852461-04-2 CAPLUS
CN 8-Azoniabicyclo[3.2.1]octane, 8-(4-chlorobutyl)-3-(2-cyano-2,2-diphenylethyl)-8-methyl-, bromide, (3-endo,8-syn)- (9CI) (CA INDEX NAME)

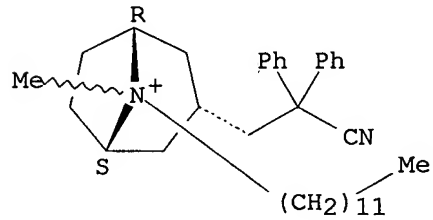
Relative stereochemistry.




● $Br^-$

RN 852461-05-3 CAPLUS
CN 8-Azoniabicyclo[3.2.1]octane, 3-(2-cyano-2,2-diphenylethyl)-8-dodecyl-8-methyl-, bromide, (3-endo,8-syn)- (9CI) (CA INDEX NAME)

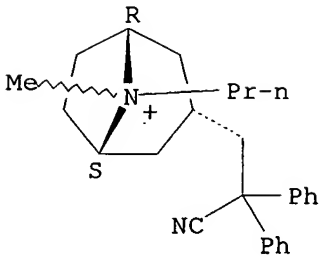
Relative stereochemistry.




● $Br^-$

RN 852461-10-0 CAPLUS
CN 8-Azoniabicyclo[3.2.1]octane, 3-(2-cyano-2,2-diphenylethyl)-8-methyl-8-propyl-, bromide, (3-endo,8-syn)- (9CI) (CA INDEX NAME)

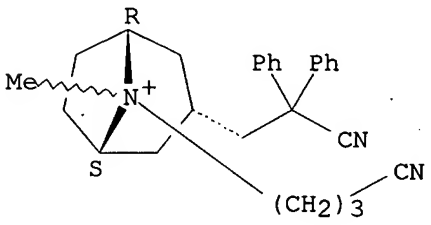
Relative stereochemistry.




● $Br^-$

RN 852461-12-2 CAPLUS
CN 8-Azoniabicyclo[3.2.1]octane, 3-(2-cyano-2,2-diphenylethyl)-8-(3-cyanopropyl)-8-methyl-, bromide, (3-endo,8-syn)- (9CI) (CA INDEX NAME)

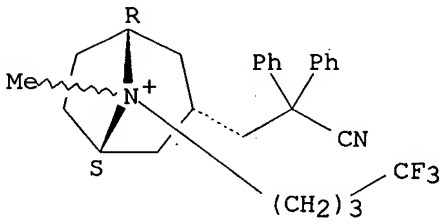
Relative stereochemistry.




● $Br^-$

RN 852461-18-8 CAPLUS
CN 8-Azoniabicyclo[3.2.1]octane, 3-(2-cyano-2,2-diphenylethyl)-8-methyl-8-(4,4,4-trifluorobutyl)-, bromide, (3-endo,8-syn)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

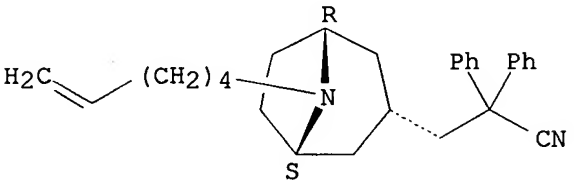



● $Br^-$

IT 852435-97-3P 852435-99-5P 852436-00-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of azabicyclo[3.2.1]octane derivs. useful as M3 muscarinic acetylcholine receptor antagonists)
RN 852435-97-3 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-propanenitrile, 8-(5-hexenyl)-α,α-

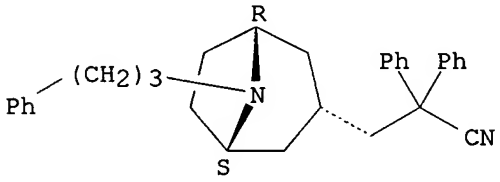
diphenyl-, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



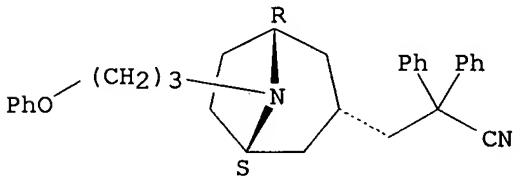
RN 852435-99-5 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-propanenitrile, α,α-diphenyl-8-(3-phenylpropyl)-, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 852436-00-1 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-propanenitrile, 8-(3-phenoxypropyl)-α,α-diphenyl-, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:878395 CAPLUS
DOCUMENT NUMBER: 141:366230
TITLE: Preparation of heterocyclylalkylbenzazolidinones as muscarinic M1 and M4 agonists.
INVENTOR(S): Kelly, Nicholas Michael; Koch, Kristian Norup; Tolf, Bo-Ragnar
PATENT ASSIGNEE(S): Acadia Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004089942 | A2 | 20041021 | WO 2004-US9859 | 20040330 |
| WO 2004089942 | A3 | 20041125 | | |

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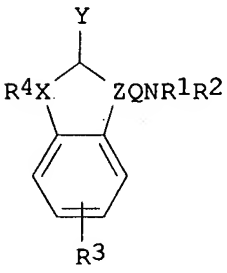
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| US 2003100545 | A1 | 20030529 | US 2002-262517 | 20020930 |
| US 7087593 | B2 | 20060808 | | |
| US 2004067931 | A1 | 20040408 | US 2003-408192 | 20030403 |
| US 6951849 | B2 | 20051004 | | |

| | | |
|---|---|---|
| PRIORITY APPLN. INFO.: | US 2001-326754P | P 20011002 |
| | US 2002-262517 | A 20020930 |
| | US 2003-406750 | A2 20030402 |
| | US 2003-408192 | A2 20030403 |

OTHER SOURCE(S): MARPAT 141:366230

GI



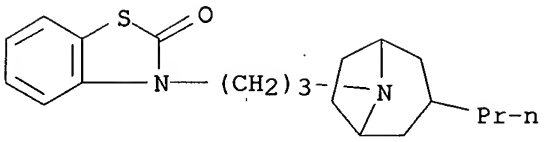

I

AB Title compds. [I; X = C, O, N, S; Z = CH, N; Y = O, N, S, tautomers thereof; Q = (CR6R7)nA,(CR6R7)p-CH=CH-(CR6R7)q, etc.; n, p, q = 0-5; A = null, C3-8 cycloalkyl; NR1R2 = (substituted) perhydroazocinyl, perhydroazepinyl, piperidinyl, pyrrolidinyl, azetidinyl, aziridinyl, 8-azabicyclo[3.2.1]octyl; R3 = 0-4 of halo, OH, (substituted) alkyl, alkoxy, alkylidene, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, alkylcarbonyl; R4 = H, (substituted) alkyl, cycloalkyl, alkenyl, alkynyl, aminomethyl, alkoxymethyl, alkylthiomethyl, etc.; R6, R7 = H, halo, OH, (substituted) alkyl, alkoxy, heteroalkyl, alkylidene, alkenyl, alkynyl, aryl, etc.], were prepared Thus, 3-(2-chloroethyl)-3H-benzothiazol-2-one (preparation given), 4-butylpiperidine, NaI, and K2CO3 were shaken in MeCN at 50° for 20 h to give 13% 3-[2-(4-butylpiperidin-1-yl)ethyl]-3H-benzothiazol-2-one. Tested I gave 63-115% efficacy at M1 receptors relative to carbachol.

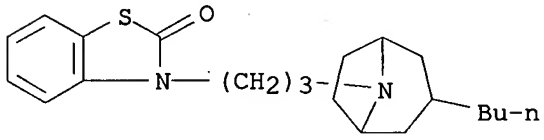
IT 509147-52-8P 509147-53-9P 509147-54-0P
509147-55-1P 676367-01-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzazolidinones as muscarinic M1 and M4 agonists)

RN 509147-52-8 CAPLUS

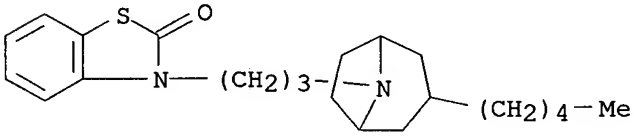
CN 2(3H)-Benzothiazolone, 3-[3-(3-propyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]-(9CI) (CA INDEX NAME)



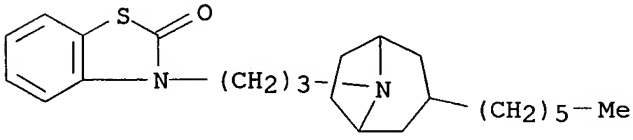
RN 509147-53-9 CAPLUS
CN 2(3H)-Benzothiazolone, 3-[3-(3-butyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]- (9CI) (CA INDEX NAME)



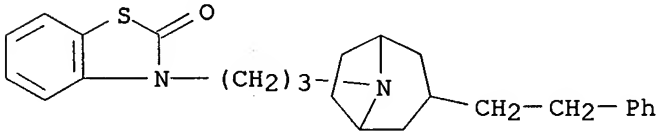
RN 509147-54-0 CAPLUS
CN 2(3H)-Benzothiazolone, 3-[3-(3-pentyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]- (9CI) (CA INDEX NAME)



RN 509147-55-1 CAPLUS
CN 2(3H)-Benzothiazolone, 3-[3-(3-hexyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]- (9CI) (CA INDEX NAME)



RN 676367-01-4 CAPLUS
CN 2(3H)-Benzothiazolone, 3-[3-[3-(2-phenylethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:293387 CAPLUS
DOCUMENT NUMBER: 140:303675
TITLE: Preparation of heterocyclylalkylbenzazolidinones as muscarinic M1 and M4 agonists.
INVENTOR(S): Kelly, Nicholas Michael; Koch, Kristian Norup; Tolf,

Bo-Ragnar
PATENT ASSIGNEE(S): Acadia Pharmaceuticals, Inc., Den.
SOURCE: U.S. Pat. Appl. Publ., 48 pp., Cont.-in-part of U.S. Ser. No. 262,517.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004067931 | A1 | 20040408 | US 2003-408192 | 20030403 |
| US 6951849 | B2 | 20051004 | | |
| US 2003100545 | A1 | 20030529 | US 2002-262517 | 20020930 |
| US 7087593 | B2 | 20060808 | | |
| WO 2004089942 | A2 | 20041021 | WO 2004-US9859 | 20040330 |
| WO 2004089942 | A3 | 20041125 | | |
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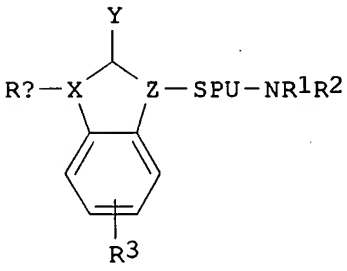
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2006025402 | A1 | 20060202 | US 2005-188295 | 20050721 |
| US 2006199799 | A1 | 20060907 | US 2006-418340 | 20060503 |
| US 2006205785 | A1 | 20060914 | US 2006-418342 | 20060503 |
| US 2006258707 | A1 | 20061116 | US 2006-490416 | 20060719 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 2001-326754P | P | 20011002 |
| US 2002-262517 | A2 | 20020930 |
| US 2003-406750 | A2 | 20030402 |
| US 2003-408192 | A2 | 20030403 |
| US 2005-188295 | A1 | 20050721 |

OTHER SOURCE(S): MARPAT 140:303675
GI

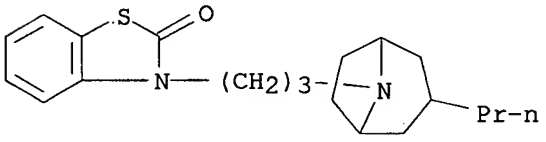



I

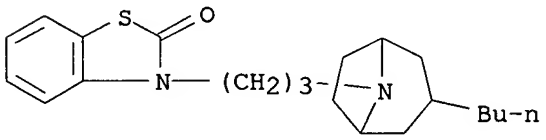
AB Title compds. [I; X = C, O, N, S; Z = CH, N; Y = O, N, S, tautomers thereof; SPU = spacer; N together with R1-2 form a heterocycle; R3 present 0-4 times = halo, OH, alkyl, etc.; Rx = absent, H, alkyl, etc.], are prepared Thus, 3-(2-chloroethyl)-3H-benzothiazol-2-one (preparation given), 4-butylpiperidine, NaI, and K2CO3 were shaken in MeCN at 50° for 20 h to give 13% 3-[2-(4-butylpiperidin-1-yl)ethyl]-3H-benzothiazol-2-one. Tested I gave 63-115% efficacy at M1 receptors relative to carbachol.

IT 509147-52-8P 509147-53-9P 509147-54-0P
509147-55-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzazolidinones as muscarinic M1 and M4 agonists)

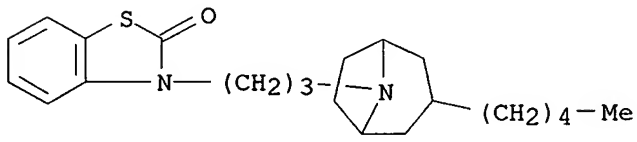
RN 509147-52-8 CAPLUS
CN 2(3H)-Benzothiazolone, 3-[3-(3-propyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]- (9CI) (CA INDEX NAME)



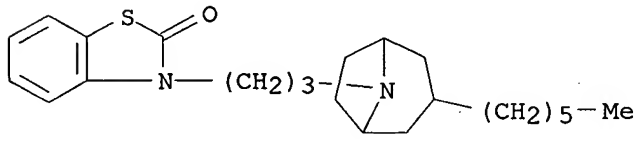

RN 509147-53-9 CAPLUS
CN 2(3H)-Benzothiazolone, 3-[3-(3-butyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]- (9CI) (CA INDEX NAME)




RN 509147-54-0 CAPLUS
CN 2(3H)-Benzothiazolone, 3-[3-(3-pentyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]- (9CI) (CA INDEX NAME)

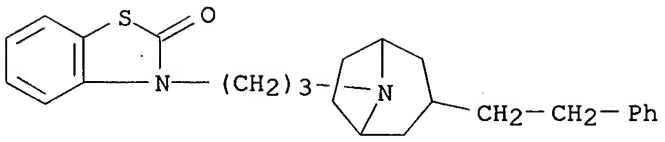



RN 509147-55-1 CAPLUS
CN 2(3H)-Benzothiazolone, 3-[3-(3-hexyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]- (9CI) (CA INDEX NAME)




IT 676367-01-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclylalkylbenzazolidinones as muscarinic M1 and M4 agonists)

RN 676367-01-4 CAPLUS
CN 2(3H)-Benzothiazolone, 3-[3-[3-(2-phenylethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

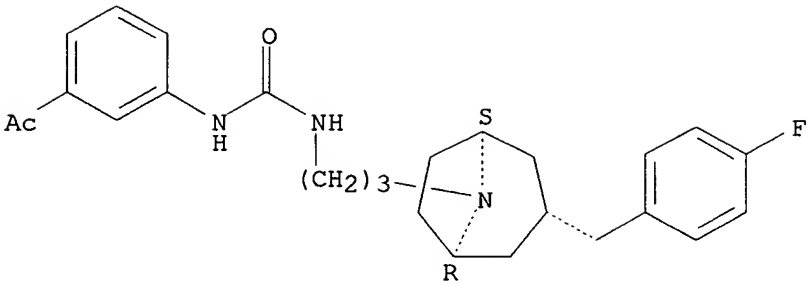
L4 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:214100 CAPLUS
DOCUMENT NUMBER: 141:396
TITLE: Discovery of N-propylurea 3-benzylpiperidines as selective CC chemokine receptor-3 (CCR3) antagonists
AUTHOR(S): Varnes, Jeffrey G.; Gardner, Daniel S.; Santella, Joseph B.; Duncia, John V.; Estrella, Melissa; Watson, Paul S.; Clark, Cheryl M.; Ko, Soo S.; Welch, Patricia; Covington, Maryanne; Stowell, Nicole; Wadman, Eric; Davies, Paul; Solomon, Kimberley; Newton, Robert C.; Trainor, George L.; Decicco, Carl P.; Wacker, Dean A.
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08542-5400, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(7), 1645-1649
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:396

AB The discovery of novel and selective small mol. antagonists of the CC chemokine receptor-3 (CCR3) is presented. Simple conversion from a 4- to 3-benzylpiperidine gave improved selectivity for CCR3 over the serotonin 5HT2A receptor. Chiral resolution and exploration of mono- and disubstitution of the N-propylurea resulted in several 3-benzylpiperidine N-propylureas with CCR3 binding IC50s under 5 nM. Data from in vitro calcium mobilization and chemotaxis assays for these compds. ranged from high picomolar to low nanomolar EC50s and correlated well with antagonist binding IC50s.

IT 693256-78-9P 693788-77-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(discovery of propylurea benzylpiperidines as selective CCR3 antagonists)

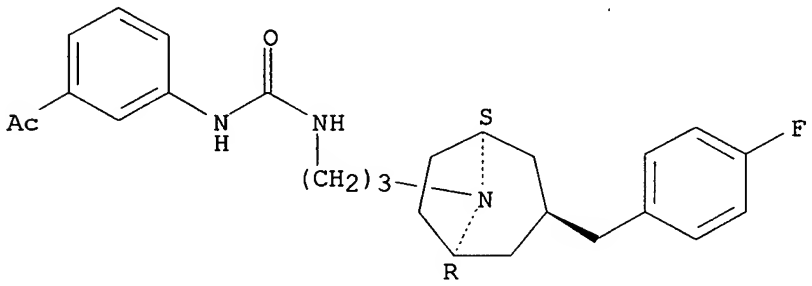
RN 693256-78-9 CAPLUS
CN Urea, N-(3-acetylphenyl)-N'-[3-[(3-exo)-3-[(4-fluorophenyl)methyl]-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 693788-77-1 CAPLUS
CN Urea, N-(3-acetylphenyl)-N'-[3-[(3-endo)-3-[(4-fluorophenyl)methyl]-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:282333 CAPLUS
DOCUMENT NUMBER: 138:304284
TITLE: Preparation of heterocyclylalkylbenzazolidinones as muscarinic M1 and M4 agonists.
INVENTOR(S): Kelly, Nicholas Michael; Koch, Kristian Norup; Tolf, Bo-ragnar
PATENT ASSIGNEE(S): Acadia Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

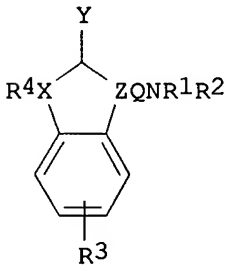
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003028650 | A2 | 20030410 | WO 2002-US31308 | 20020930 |
| WO 2003028650 | A3 | 20030619 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| AU 2002327810 | A1 | 20030414 | AU 2002-327810 | | 20020930 |
| EP 1432420 | A2 | 20040630 | EP 2002-763824 | | 20020930 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | | |
| CN 1561212 | A | 20050105 | CN 2002-819444 | | 20020930 |
| JP 2005510473 | T | 20050421 | JP 2003-531986 | | 20020930 |
| BR 2002013611 | A | 20051220 | BR 2002-13611 | | 20020930 |
| RU 2288919 | C2 | 20061210 | RU 2004-113451 | | 20020930 |
| NZ 531550 | A | 20061222 | NZ 2002-531550 | | 20020930 |
| NO 2004001317 | A | 20040629 | NO 2004-1317 | | 20040330 |
| ZA 2004002609 | A | 20050509 | ZA 2004-2609 | | 20040401 |
| PRIORITY APPLN. INFO.: | | | US 2001-326754P | P | 20011002 |
| | | | WO 2002-US31308 | W | 20020930 |

OTHER SOURCE(S): MARPAT 138:304284

GI



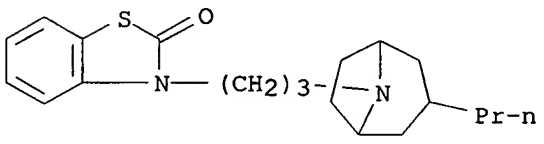

I

AB Title compds. [I; X = C, O, N, S; Z = CH, N; Y = O, N, S, tautomers thereof; Q = (CR6R7)nA, C3-8 cycloalkyl; n = 1-5; A = null, C3-8 cycloalkyl; NR1R2 = (substituted) perhydroazocinyl, perhydroazepinyl, piperidinyl, pyrrolidinyl, azetidinyl, aziridinyl, 8-azabicyclo[3.2.1]octyl; R3 = 0-4 of halo, OH, (substituted) alkyl, alkoxy, alkylidene, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, alkylcarbonyl; R4 = H, (substituted) alkyl, cycloalkyl, alkenyl, alkynyl, aminomethyl, alkoxymethyl, alkylthiomethyl, etc.], were prepared Thus, 3-(2-chloroethyl)-3H-benzothiazol-2-one (preparation given), 4-butylpiperidine, NaI, and K2CO3 were shaken in MeCN at 50° for 20 h to give 13% 3-[2-(4-butylpiperidin-1-yl)ethyl]-3H-benzothiazol-2-one. Tested I gave 63-115% efficacy at M1 receptors relative to carbachol.

IT 509147-52-8P 509147-53-9P 509147-54-0P
509147-55-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzazolidinones as muscarinic M1 and M4 agonists)

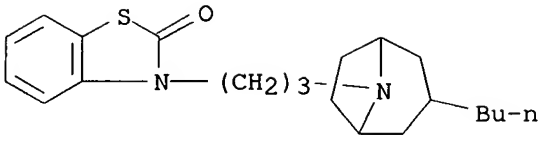
RN 509147-52-8 CAPLUS

CN 2(3H)-Benzothiazolone, 3-[3-(3-propyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]- (9CI) (CA INDEX NAME)

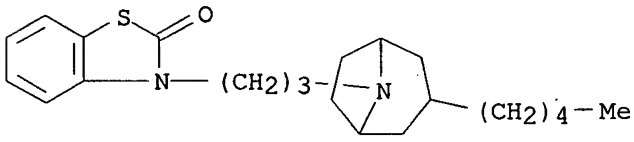



RN 509147-53-9 CAPLUS

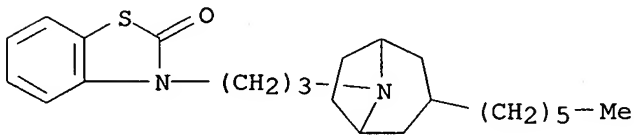
CN 2(3H)-Benzothiazolone, 3-[3-(3-butyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]- (9CI) (CA INDEX NAME)



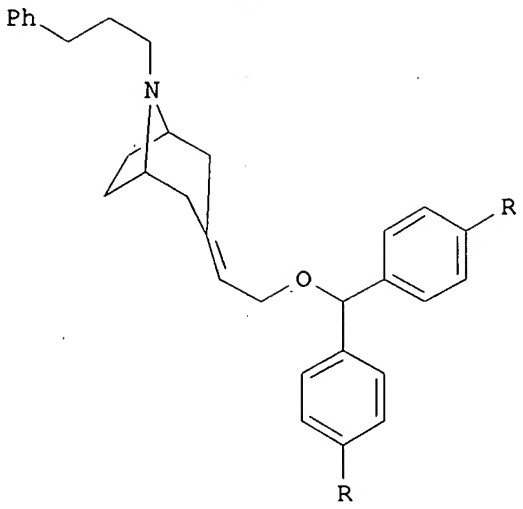
RN 509147-54-0 CAPLUS
CN 2(3H)-Benzothiazolone, 3-[3-(3-pentyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]- (9CI) (CA INDEX NAME)



RN 509147-55-1 CAPLUS
CN 2(3H)-Benzothiazolone, 3-[3-(3-hexyl-8-azabicyclo[3.2.1]oct-8-yl)propyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:189370 CAPLUS
DOCUMENT NUMBER: 139:52839
TITLE: Synthesis of dopamine transporter selective 3-{2-(Diarylmethoxyethylidene)}-8-alkylaryl-8-azabicyclo[3.2.1]octanes
AUTHOR(S): Bradley, Amy L.; Izenwasser, Sari; Wade, Dean; Cararas, Shaine; Trudell, Mark L.
CORPORATE SOURCE: Department of Chemistry, University of New Orleans, New Orleans, LA, 70148, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(4), 629-632
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:52839
GI



I

AB A series of 3-{2-(diarylmethoxyethylidene)}-8-alkylaryl-8-azabicyclo[3.2.1]octanes was synthesized and the binding affinities of the compds. were determined at the dopamine and serotonin transporters. The 8-phenylpropyl analogs I [R = H (Ki=4.1 nM); R = F (Ki=3.7 nM)] were the most potent compds. of the series with binding affinities 3 times greater than GBR-12909. In addition, I (R = H; SERT/DAT=327) was over 300-fold more selective for the dopamine transporter than the serotonin transporter.

IT 548459-04-7P 548459-06-9P 548459-08-1P
548459-10-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(stereoselective preparation, dopamine and serotonin transporter affinities, and SAR of (diarylmethoxyethyl)azabicyclooctanes via reduction of azabicyclooctaneacetate followed by alkylation with benzhydryl chlorides)

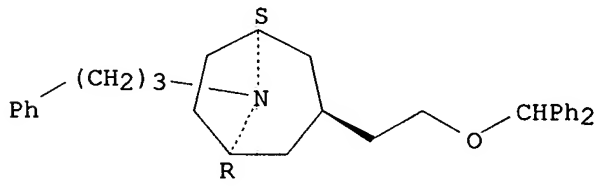
RN 548459-04-7 CAPLUS

CN 8-Azabicyclo[3.2.1]octane, 3-[2-(diphenylmethoxy)ethyl]-8-(3-phenylpropyl)-, (3-endo)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

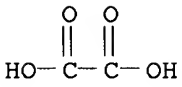
CRN 548459-03-6
CMF C31 H37 N O

Relative stereochemistry.



CM 2

CRN 144-62-7
CMF C2 H2 O4

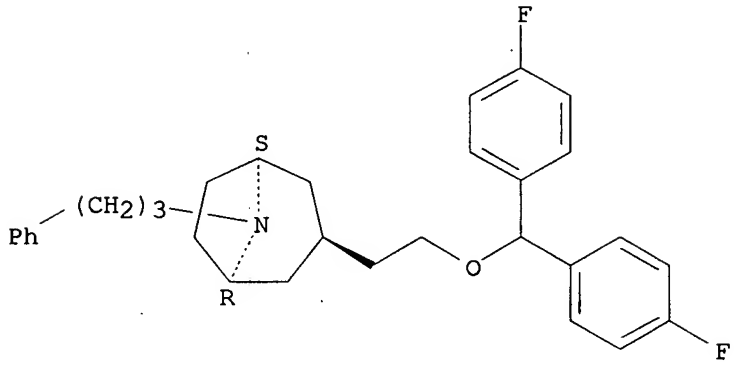


RN 548459-06-9 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[2-[bis(4-fluorophenyl)methoxy]ethyl]-8-(3-phenylpropyl)-, (3-endo)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

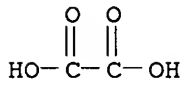
CRN 548459-05-8
CMF C31 H35 F2 N O

Relative stereochemistry.



CM 2

CRN 144-62-7
CMF C2 H2 O4

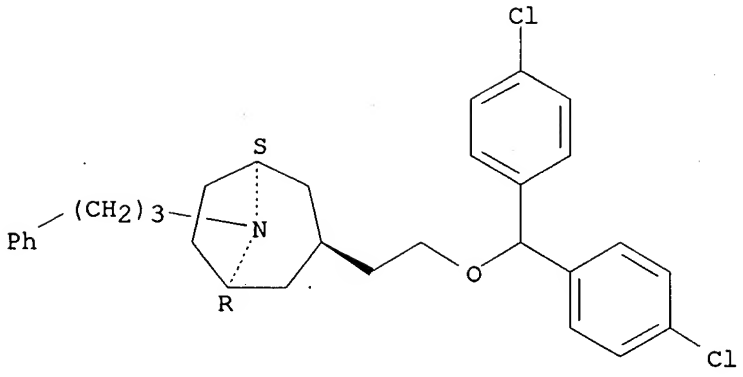


RN 548459-08-1 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[2-[bis(4-chlorophenyl)methoxy]ethyl]-8-(3-phenylpropyl)-, (3-endo)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

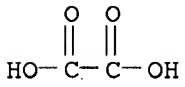
CRN 548459-07-0
CMF C31 H35 Cl2 N O

Relative stereochemistry.




CM 2

CRN 144-62-7
CMF C2 H2 O4

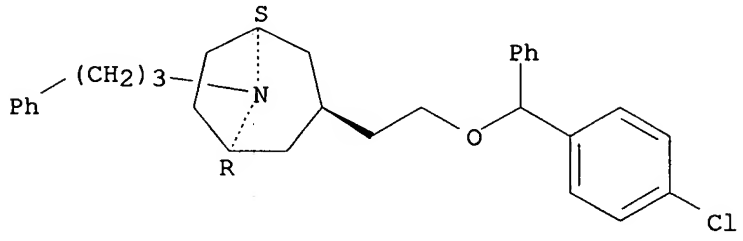



RN 548459-10-5 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[2-[(4-chlorophenyl)phenylmethoxy]ethyl]-8-(3-phenylpropyl)-, (3-endo)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

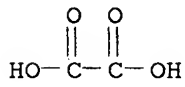
CRN 548459-09-2
CMF C31 H36 Cl N O

Relative stereochemistry.




CM 2

CRN 144-62-7
CMF C2 H2 O4

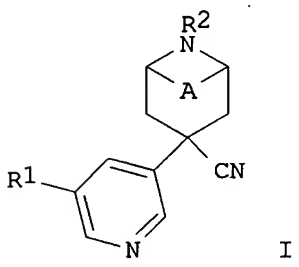



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:98104 CAPLUS
DOCUMENT NUMBER: 138:137175
TITLE: Preparation of 3-cyano-3-pyridylazabicyclo[3.2.1]octanes as insecticides, acaricides, and nematocides.
INVENTOR(S): Salmon, Roger
PATENT ASSIGNEE(S): Syngenta Limited, UK
SOURCE: Brit. UK Pat. Appl., 25 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 2378181 | A | 20030205 | GB 2002-15429 | 20020703 |
| PRIORITY APPLN. INFO.: | | | GB 2001-17032 A | 20010712 |

OTHER SOURCE(S): MARPAT 138:137175
GI



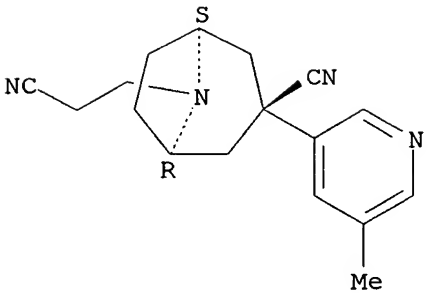
I

AB Title compds. I;. Thus, 8-benzyl-exo-3-cyano-8-azabicyclo[3.2.1]octane and 3,5-dibromopyridine in THF were treated with Li(SiMe3)2 to give 8-benzyl-exo-3-(5-bromopyrid-3-yl)-endo-3-cyano-8-azabicyclo[3.2.1]octane. The latter with MeI in Et2O/THF at -30° was treated with MeLi followed by warming to room temperature to give 8-benzyl-endo-3-cyano-exo-3-(5-methylpyrid-3-yl)-8-azabicyclo[3.2.1]octane. Several I at 500 ppm gave 80-100% control of Myzus persicae on cabbage leaves.

IT 494767-63-4P
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyanopyridylazabicyclooctanes as insecticides, acaricides, and nematocides)

RN 494767-63-4 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-8-propanenitrile, 3-cyano-3-(5-methyl-3-pyridinyl)-, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.




REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:59634 CAPLUS
DOCUMENT NUMBER: 138:73416
TITLE: Preparation of pyridinyl-8-azabicyclics for use as pesticides
INVENTOR(S): Salmon, Roger; Bacon, David Philip
PATENT ASSIGNEE(S): Syngenta Limited, UK
SOURCE: Brit. UK Pat. Appl., 27 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 2372744 | A | 20020904 | GB 2002-823 | 20020115 |
| PRIORITY APPLN. INFO.: | | | GB 2001-1226 A | 20010117 |
| OTHER SOURCE(S): | MARPAT 138:73416 | | | |

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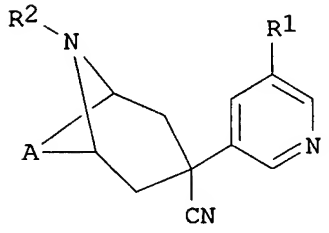
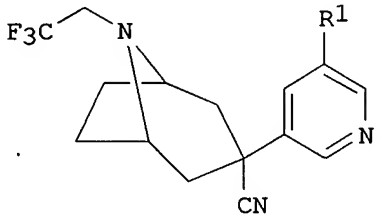



I




II

AB Pyridinyl substituted azabicyclic compds., such as I [A = CH2CH2, CH:CH; R1 = C2-10-alkynyl; R2 = H, CHO, carboxyl, alkyl, alkoxy, alkenyloxy, aryl, heteroaryl, etc.]. Thus, endo-3-cyano-8-(2,2,2-trifluoroethyl)-exo-3-[5-(trimethylsilylethynyl)pyrid-3-yl]-8-azabicyclo[3.2.1]octane II (R1 = C.tplbond.CSiMe3) was prepared by reaction of HC.tplbond.CSiMe3 with the corresponding bromide II (R1 = Br) using (Ph3P)2PdCl2, CuI and Et3N in a sealed glass carius tube and heated to 60° for 18 h. The prepared azabicyclics were assayed for their insecticidal activity against peach aphid, i.e. Myzus persicae, by determining mortality rate of a 500 ppm by weight composition of each of the azabicyclics in an acetone/ethanol/water solution

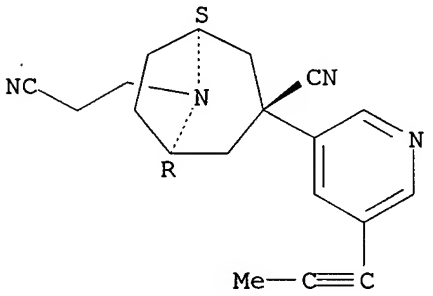
IT 481696-05-3P 481696-14-4P 481696-15-5P
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of pyridinyl-8-azabicyclo[3.2.1]octanes for use as pesticides)

RN 481696-05-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-8-propanenitrile, 3-cyano-3-[5-(1-propynyl)-3-pyridinyl]-, (3-endo)- (9CI) (CA INDEX NAME)

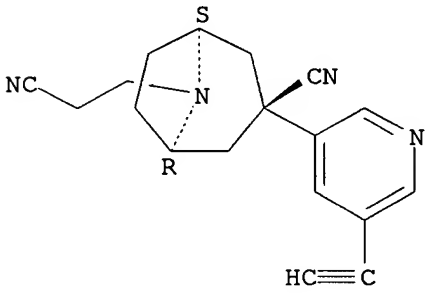
Relative stereochemistry.




RN 481696-14-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-8-propanenitrile, 3-cyano-3-(5-ethynyl-3-pyridinyl)-, (3-endo)- (9CI) (CA INDEX NAME)

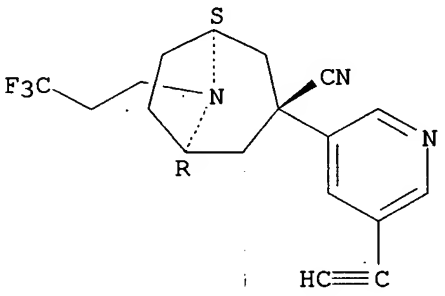
Relative stereochemistry.




RN 481696-15-5 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-3-carbonitrile, 3-(5-ethynyl-3-pyridinyl)-8-(3,3,3-trifluoropropyl)-, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.




L4 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:555491 CAPLUS

DOCUMENT NUMBER: 137:109215

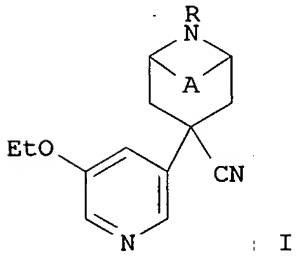
TITLE: Preparation of 8-azabicyclo[3.2.1]octanes as insecticides

INVENTOR(S): Salmon, Roger

PATENT ASSIGNEE(S): Syngenta Limited, UK
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002057263 | A1 | 20020725 | WO 2002-GB154 | 20020115 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002219384 | A1 | 20020730 | AU 2002-219384 | 20020115 |
| PRIORITY APPLN. INFO.: | | | GB 2001-1229 A | 20010117 |
| | | | GB 2001-17033 A | 20010712 |
| | | | WO 2002-GB154 W | 20020115 |

OTHER SOURCE(S): MARPAT 137:109215
GI



I

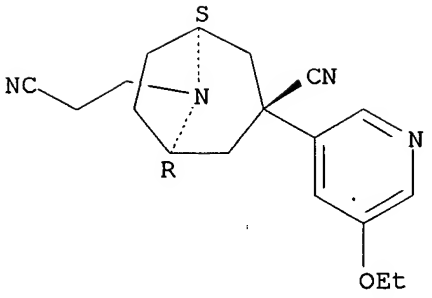
AB The title compds. I (A = CH2-CH2- or -CH=CH-; R = H, CHO, COOC1-C10 alkyl, optionally substituted C2-C10 alkyl, substituted Me, optionally substituted C1-C10 alkoxy, optionally substituted C2-C10 alkenyloxy, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C2-C10 alkenyl, optionally substituted C3-C10 alkynyl or optionally substituted C3-C7 cycloalkyl) and their acid addition salts, quaternary ammonium salts, salts and N-oxides were prepared as insecticides. Thus, 8-benzyl-exo-3-(5-chloro-3-pyridyl)-endo-3-cyano-8-azabicyclo[3.2.1]octane was treated with EtONa to give 8-benzyl-exo-3-(5-ethoxy-3-pyridyl)-endo-3-cyano-8-azabicyclo[3.2.1]octane (II). II had 80-100% mortality against Myzus persicae at 500 ppm.

IT 443640-57-1P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of 8-azabicyclo[3.2.1]octanes as insecticides)

RN 443640-57-1 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-8-propanenitrile, 3-cyano-3-(5-ethoxy-3-pyridinyl)-, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

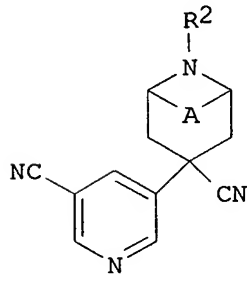



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:555490 CAPLUS
DOCUMENT NUMBER: 137:125100
TITLE: Bicyclic amines as insecticides
INVENTOR(S): Salmon, Roger
PATENT ASSIGNEE(S): Syngenta Limited, UK
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002057262 | A2 | 20020725 | WO 2002-GB152 | 20020115 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002219383 | A1 | 20020730 | AU 2002-219383 | 20020115 |
| PRIORITY APPLN. INFO.: | | | GB 2001-1228 A | 20010117 |
| | | | GB 2001-17035 A | 20010712 |
| | | | WO 2002-GB152 W | 20020115 |

OTHER SOURCE(S): MARPAT 137:125100
GI




I

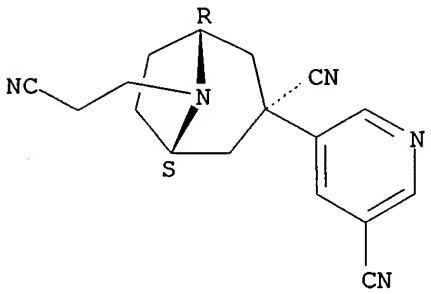
AB A compound of formula (I) wherein A is -CH2-CH2- or -CH=CH-; R2 is hydrogen, CHO, COOC1-C10 alkyl, optionally substituted C2-C10 alkyl, substituted Me, optionally substituted C1-C10 alkoxy, optionally substituted C2-C10 alkenyloxy, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted C2-C10 alkenyl, optionally substituted C3-C10 alkynyl or optionally substituted C3-C7 cycloalkyl; and acid addition salts, quaternary ammonium salts and N-oxides derived therefrom. The compds. are useful as insecticides.

IT 443925-07-3P
RL: AGR (Agricultural use); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(insecticide; preparation of bicyclic amines as insecticides)

RN 443925-07-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-8-propanenitrile, 3-cyano-3-(5-cyano-3-pyridinyl)-, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.




L4 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:256232 CAPLUS

DOCUMENT NUMBER: 136:294857

TITLE: Preparation of nitrogen-containing compounds as the active ingredient of CCR3 inhibitors

INVENTOR(S): Takahashi, Toshiya; Imaoka, Takayuki; Tomioka, Hiroki; Hatakeyama, Daigo; Nitta, Aiko; Kaneko, Masayuki; Takizawa, Satoko; Torii, Yuichi; Morihira, Koichiro; Morokata, Tatsuaki

PATENT ASSIGNEE(S): Toray Industries, Inc., Japan

SOURCE: PCT Int. Appl., 146 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

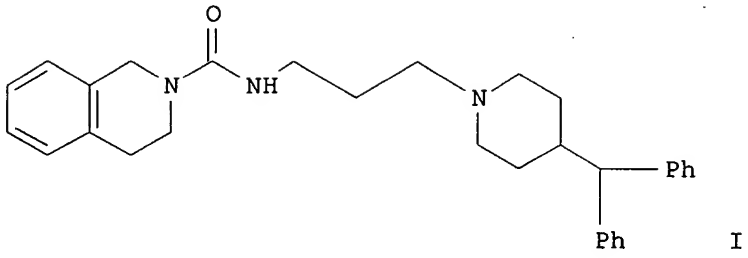
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002026708 | A1 | 20020404 | WO 2001-JP8466 | 20010927 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| JP 2002187880 | A | 20020705 | JP 2001-293350 | 20010926 |
| AU 2001092276 | A5 | 20020408 | AU 2001-92276 | 20010927 |
| PRIORITY APPLN. INFO.: | | | JP 2000-294355 A | 20000927 |

JP 2000-313405 A 20001013
WO 2001-JP8466 W 20010927

OTHER SOURCE(S): MARPAT 136:294857
GI



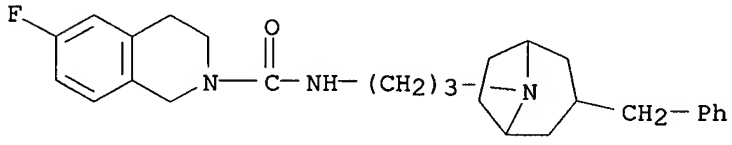
I

AB Title compds. [Ar(CH2)nA(CH2)m(Y)xBB1; Ar = (un)substituted-1,2,3,4-tetrahydroisoquinoline-2-yl, 3-substituted-pyrimidine-2-one-1-yl, C6H5CH2NHCH2CH2NH, 3-benzyl-imidazole-2-one-1-yl, 1,3-dihydro-isoindole-2-yl, C6H5, CONH(CH2)3; C(NH)NH(CH2)3, CO, N(CH3)C(:NH)NH(CH2)3, N(CH3)C(:NH)NHCH2CH2, n = 0, 1, 2, 3; A = 1-piperidinyl, 1-piperazinyl, 1-homopiperazinyl; m = 0, 1, 2, 3; x = 0, 1; Y = CO, SO2; B = H, (un)substituted-aryl, (un)substituted-heterocyclyl; B1 = (un)substituted-aryl, electron pair, etc] and pharmaceutically acceptable salts are prepared and are useful as CCR3 inhibitors to be used in preventing and treating allergic inflammatory diseases caused by leukergy of lymphocytes, eosinocytes, basophilic leukocytes. Thus, the title compound I was prepared with 54% yield from 1,2,3,4-tetrahydroisoquinoline-2-carbonyl chloride and 3-(4-(diphenylmethyl)piperidinyl)propylamine in THF at room temperature for 4 h. The title compound I was tested for CCR3 inhibition (IC50 = 2.1 μM) with B300-19 cells.

IT 406923-49-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrogen-containing compds. as the active ingredient of CCR3 inhibitors)

RN 406923-49-7 CAPLUS

CN 2(1H)-Isoquinolinecarboxamide, 6-fluoro-3,4-dihydro-N-[3-[3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

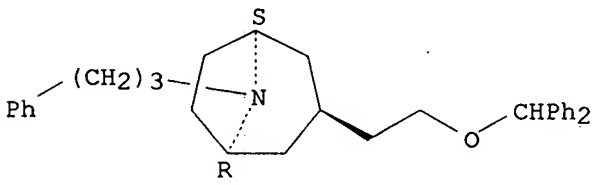
L4 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:749720 CAPLUS
DOCUMENT NUMBER: 136:37802
TITLE: Synthesis and biological evaluation of tropane-like 1-{2-[bis(4-fluorophenyl)methoxy]ethyl}-4-(3-phenylpropyl)piperazine (GBR 12909) analogs

AUTHOR(S): Zhang, Ying; Joseph, David B.; Bowen, Wayne D.; Flippen-Anderson, Judith L.; Dersch, Christina M.; Rothman, Richard B.; Jacobson, Arthur E.; Rice, Kenner C.
CORPORATE SOURCE: Laboratory of Medicinal Chemistry National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0815, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(23), 3937-3945
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:37802
AB The authors have prepared azabicyclo[3.2.1] derivs. (C-3-substituted tropanes) that bind with high affinity to the dopamine transporter and inhibit dopamine reuptake. Within the series, 3-{2-[bis-(4-fluorophenyl)methoxy]ethylidene}-8-methyl-8-azabicyclo[3.2.1]octane (I) was found to have the highest affinity and selectivity for the dopamine transporter. These azabicyclo[3.2.1] (bridged piperidine) series of compds. differ from the well-known benztropines by a 2-carbon spacer between C-3 and a diarylmethoxy moiety. Interestingly, these new compds. demonstrated a much lower affinity for the muscarinic-1 site, at least a 100-fold decrease compared to benztropine. Interestingly, these new compds. demonstrated a much lower affinity for the muscarinic-1 site, at least a 100-fold decrease compared to benztropine. Replacing N-Me with N-phenylpropyl in two of the compds. resulted in a 3-10-fold increase in binding affinity for the dopamine transporter. However, those compds. lost selectivity for the dopamine transporter over the serotonin transporter. Replacement of the ether oxygen in the diarylmethoxy moiety with a nitrogen atom gave relatively inactive amines, indicating the important role which is played by the ether oxygen in transporter binding. Reduction of the C-3 double bond in I gave 3α-substituted tropanes, as shown by X-ray crystallog. analyses. The 3α-substituted tropanes had lower affinity and less selectivity than the comparable unsatd. ligands.

IT 380602-02-8P 380602-03-9P
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, muscarinic M1 receptor, dopamine and serotonin transporter affinity, and structure-activity relationship of azabicyclooctane derivs. as GBR 12909 analogs)

RN 380602-02-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[2-(diphenylmethoxy)ethyl]-8-(3-phenylpropyl)-, hydrochloride, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

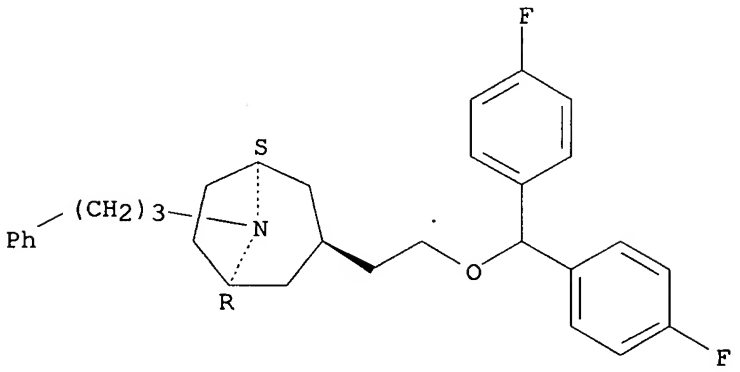



● HCl

RN 380602-03-9 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[2-[bis(4-fluorophenyl)methoxy]ethyl]-8-(3-

phenylpropyl)-, hydrochloride, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



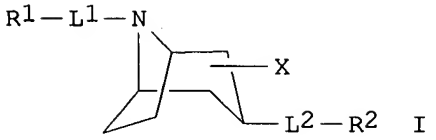

● HCl

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

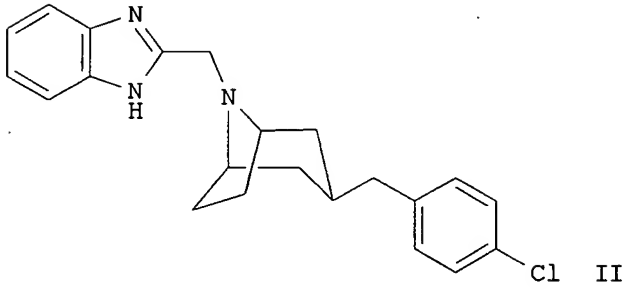
L4 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:338355 CAPLUS
DOCUMENT NUMBER: 134:340509
TITLE: Preparation of 8-azabicyclo[3.2.1]octane NMDA/NR2B antagonists
INVENTOR(S): Thompson, Wayne; Claremon, David A.; Munson, Peter M.; Phillips, Brian
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001032179 | A1 | 20010510 | WO 2000-US29479 | 20001026 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6432976 | B1 | 20020813 | US 2000-696503 | 20001025 |
| CA 2388171 | A1 | 20010510 | CA 2000-2388171 | 20001026 |
| EP 1244450 | A1 | 20021002 | EP 2000-979131 | 20001026 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003513044 | T | 20030408 | JP 2001-534384 | 20001026 |
| PRIORITY APPLN. INFO.: | | | US 1999-162718P | P 19991029 |
| | | | WO 2000-US29479 | W 20001026 |

OTHER SOURCE(S): MARPAT 134:340509
GI



I



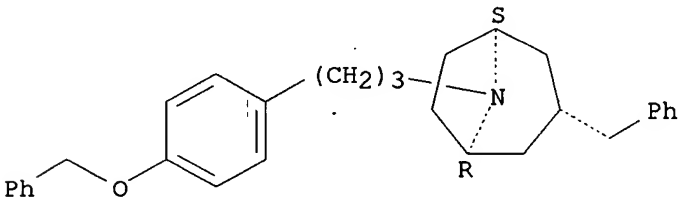
II

AB The title compds., commonly known as tropanes, (I) [wherein R1 = (un)substituted 2-benzimidazole, imidazole, imidazopyridine, indole, quinazoline, purine, benzoxazolone, or phenol; R2 = Ph, optionally substituted with 1-5 substituents selected from Cl, F, Br, alkyl, CF3, OH, or CO2H; L1 and L2 = independently (cyclo)alkyl, alkenyl, alkynyl, alkoxy, aminoalkyl, hydroxyalkyl, or (amino)carbonyl; X = OH, NH2, (di)alkylamino, alkyl, ester, carbamate, carbonate, or ether] were prepared as effective NMDA NR2B glutamate receptor antagonists. For example, addition of di-Et 4-chlorobenzylphosphonate to N-carbethoxy-4-tropinone to give the benzylidene, reduction using Pt/C, N-deprotection using HBr in AcOH, and reductive addition of 1-(trimethylsilylethoxymethyl)-1H-benzimidazole-2-carbaldehyde (2-step preparation given) using NaBH(OAc)3 in ClCH2CH2Cl afforded exo-II. Exptl. protocols for assessing the inhibition of NR1A/2B NMDA receptor activation (FLIPR assay) and determining the apparent dissociation consts. against the human NR1A/NR2B receptor (binding assay) are given (no data). I are useful for relieving pain and treating migraine, depression, anxiety, schizophrenia, Parkinson's disease, or stroke (no data).

IT 338733-30-5P 338733-34-9P 338733-35-0P 338733-37-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (benzimidazolylalkyl)tropane NMDA/NR2B antagonists for treatment of pain)

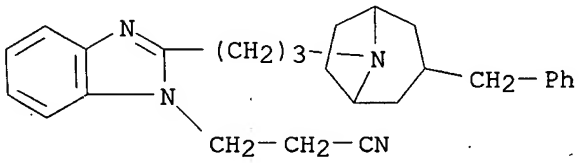
RN 338733-30-5 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 8-[3-[4-(phenylmethoxy)phenyl]propyl]-3-(phenylmethyl)-, (3-exo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

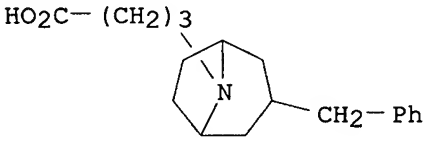


RN 338733-34-9 CAPLUS
CN 1H-Benzimidazole-1-propanenitrile, 2-[3-[3-(phenylmethyl)-8-

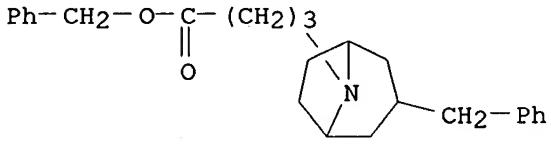
azabicyclo[3.2.1]oct-8-yl]propyl]- (9CI) (CA INDEX NAME)



RN 338733-35-0 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-8-butanoic acid, 3-(phenylmethyl)- (9CI) (CA INDEX NAME)

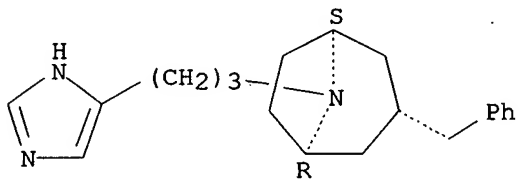


RN 338733-37-2 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-8-butanoic acid, 3-(phenylmethyl)-, phenylmethyl ester (9CI) (CA INDEX NAME)



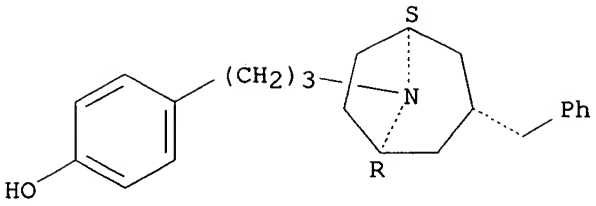
IT 338732-79-9P 338732-81-3P 338732-86-8P
338732-89-1P 338732-91-5P 338732-92-6P
338733-09-8P 338733-10-1P 338733-13-4P
338733-16-7P 338795-47-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (benzimidazolylalkyl)tropane NMDA/NR2B antagonists for treatment of pain)
RN 338732-79-9 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 8-[3-(1H-imidazol-4-yl)propyl]-3-(phenylmethyl)-, (3-exo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



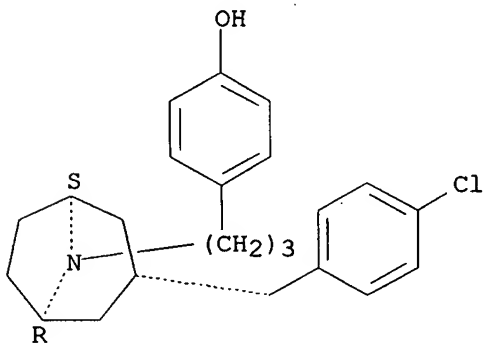
RN 338732-81-3 CAPLUS
CN Phenol, 4-[3-[(3-exo)-3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



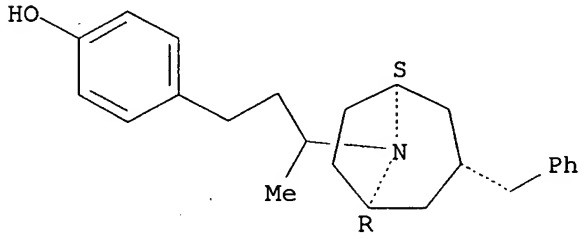

RN 338732-86-8 CAPLUS
CN Phenol, 4-[3-[(3-exo)-3-[(4-chlorophenyl)methyl]-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

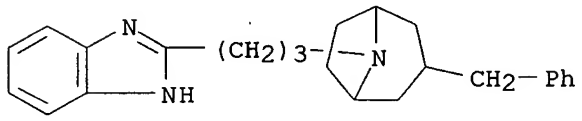



RN 338732-89-1 CAPLUS
CN Phenol, 4-[3-[(3-exo)-3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]butyl]- (9CI) (CA INDEX NAME)

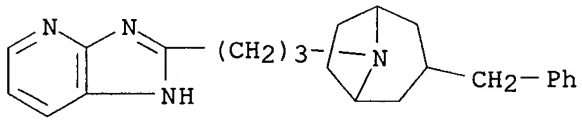
Relative stereochemistry.



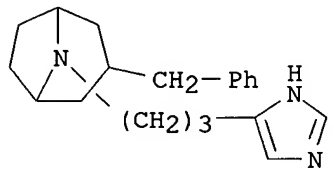

RN 338732-91-5 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 8-[3-(1H-benzimidazol-2-yl)propyl]-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



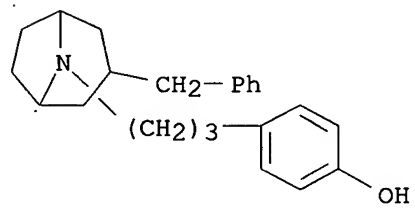

RN 338732-92-6 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 8-[3-(1H-imidazo[4,5-b]pyridin-2-yl)propyl]-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



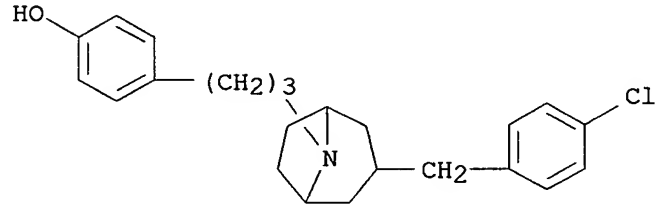
RN 338733-09-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 8-[3-(1H-imidazol-4-yl)propyl]-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



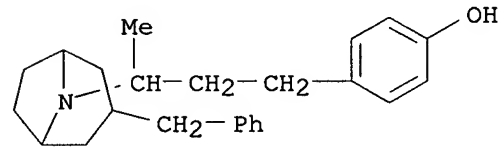
RN 338733-10-1 CAPLUS
CN Phenol, 4-[3-[3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (9CI) (CA INDEX NAME)



RN 338733-13-4 CAPLUS
CN Phenol, 4-[3-[3-[(4-chlorophenyl)methyl]-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (9CI) (CA INDEX NAME)

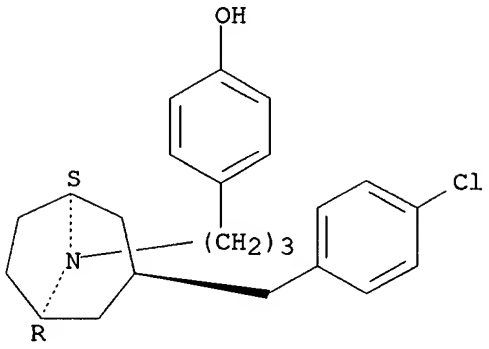


RN 338733-16-7 CAPLUS
CN Phenol, 4-[3-[3-(phenylmethyl)-8-azabicyclo[3.2.1]oct-8-yl]butyl]- (9CI) (CA INDEX NAME)



RN 338795-47-4 CAPLUS
CN Phenol, 4-[3-[(3-endo)-3-[(4-chlorophenyl)methyl]-8-azabicyclo[3.2.1]oct-8-yl]propyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.




REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:402440 CAPLUS
DOCUMENT NUMBER: 129:67708
TITLE: Preparation of 8-azabicyclo[3.2.1]octane, 8-azabicyclo[3.2.1]oct-6-ene, 9-azabicyclo[3.3.1]nonane, 9-aza-3-oxabicyclo[3.3.1]nonane, and 9-aza-3-thiabicyclo[3.3.1]nonane derivatives as insecticides
INVENTOR(S): Urch, Christopher John; Lewis, Terence; Sunley, Raymond Leo; Salmon, Raymond; Godfrey, Christopher Richard Ayles; Brightwell, Christopher Ian; et al.
PATENT ASSIGNEE(S): Zeneca Ltd., UK
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9825924 | A1 | 19980618 | WO 1997-GB3054 | 19971106 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| ZA 9709840 | A | 19980526 | ZA 1997-9840 | 19971031 |
| CA 2271749 | A1 | 19980618 | CA 1997-2271749 | 19971106 |
| AU 9748761 | A | 19980703 | AU 1997-48761 | 19971106 |
| AU 719147 | B2 | 20000504 | | |
| EP 944627 | A1 | 19990929 | EP 1997-911349 | 19971106 |
| EP 944627 | B1 | 20040218 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| BR 9713136 | A | 20000208 | BR 1997-13136 | 19971106 |
| CN 1245499 | A | 20000223 | CN 1997-181520 | 19971106 |
| SI 20020 | A | 20000229 | SI 1997-20086 | 19971106 |
| HU 200000582 | A2 | 20000628 | HU 2000-582 | 19971106 |
| JP 2001506989 | T | 20010529 | JP 1998-526332 | 19971106 |

| | | | | | |
|---|---|---|---|---|---|
| AT 259806 | T | 20040315 | AT 1997-911349 | | 19971106 |
| ES 2216131 | T3 | 20041016 | ES 1997-911349 | | 19971106 |
| US 5968947 | A | 19991019 | US 1997-969978 | | 19971113 |
| EG 21556 | A | 20011231 | EG 1997-1269 | | 19971126 |
| US 6174894 | B1 | 20010116 | US 1999-357749 | | 19990721 |
| US 6177442 | B1 | 20010123 | US 1999-357750 | | 19990721 |
| US 6291474 | B1 | 20010918 | US 2000-635879 | | 20000810 |
| US 2002061913 | A1 | 20020523 | US 2001-886495 | | 20010622 |
| PRIORITY APPLN. INFO.: | | | GB 1996-24516 | A | 19961126 |
| | | | GB 1996-24611 | A | 19961126 |
| | | | GB 1996-24614 | A | 19961126 |
| | | | WO 1997-GB3054 | W | 19971106 |
| | | | US 1997-969639 | A3 | 19971113 |
| | | | US 1997-969978 | A3 | 19971113 |
| | | | US 1999-357750 | A3 | 19990721 |
| | | | US 2000-635879 | A3 | 20000810 |

OTHER SOURCE(S): MARPAT 129:67708

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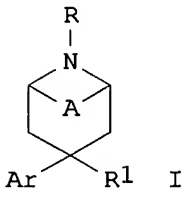



I

AB Compds. of formula [I; A = a bidentate group of the formula CH2XCH2 (wherein X = methylene, O, or S), X'C:CY or X'WCCYZ (wherein X', W, Y, Z = H, OH, acyloxy, alkoxy, alkylsilyloxy, cyano or halogen, or X' and W or Y and Z together with the carbon to which they are attached form a carbonyl group), provided that A ≠ CH2CH2; Ar = optionally substituted Ph or 5- or 6-membered heterocyclic ring system containing from 1 to 3 heteroatoms individually selected from N, O and S atoms, and at least one unsatn. (double bond) between adjacent atoms in the ring, said heterocyclic ring being optionally fused to a benzene ring; R = H or cyano or a group selected from alkyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, aralkenyl, alkynyl, alkoxycarbonyl, alkanesulfonyl, arenesulfonyl, alkenyloxycarbonyl, aralkyloxycarbonyl, aryloxycarbonyl, heterocyclylalkyl, carbamoyl, dithiocarboxyl, etc.; R1 = H, cyano, HO, alkyl, alkoxy, NH2, NO2, isocyanato, acylamino, hydroxyalkyl, optionally substituted heteroaryl, alkoxyalkyl, haloalkyl, halohydroxyalkyl, etc.; alkyl moieties of R comprise from 1 to 15 carbon atoms, and are optionally substituted with one or more substituents selected from, halogen, cyano, carboxyl, carboxyl acyl, etc.] or an acid addition salt, quaternary ammonium salt or N-oxide derived therefrom are prepared Also claimed are an insecticidal, acaricidal or nematicidal composition comprising a compound of formula I and a suitable carrier or diluent therefor and a method of combating and controlling insect, acarid or nematode pests at a locus which comprises treating the pests or the locus of the pests with an effective amount of a compound of formula I or a composition as hereinbefore described. Thus, exo-3-cyano-9-methyl-9-azabicyclo[3.3.1]nonane and 3,5-dichloropyridine (preparation given) in THF were treated dropwise with lithium bis(trimethylsilyl)amide, and the reaction mixture was allowed to react ambient temperature for 18 h to give I [A = (CH2)3, Ar = exo-5-chloropyridyl, R = Me, R1 = endo-cyano], which at 500 ppm showed 80-100% mortality against peach aphid (Myzus persicae).

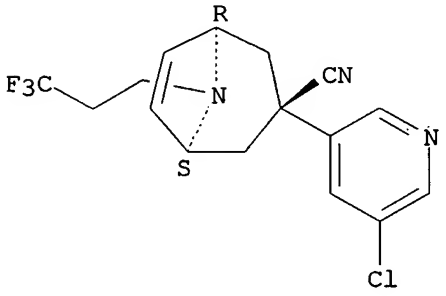
IT 209054-33-1P 209054-36-4P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic

preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azabicyclo[3.2.1]octane, azabicyclo[3.2.1]octene, azabicyclo[3.3.1]nonane, azaoxabicyclo[3.3.1]nonane, and azathiabicyclo[3.3.1]nonane derivs. as insecticides, nematocides, and acaricides)

RN 209054-33-1 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-6-ene-3-carbonitrile, 3-(5-chloro-3-pyridinyl)-8-(3,3,3-trifluoropropyl)-, (3-endo)- (9CI) (CA INDEX NAME)

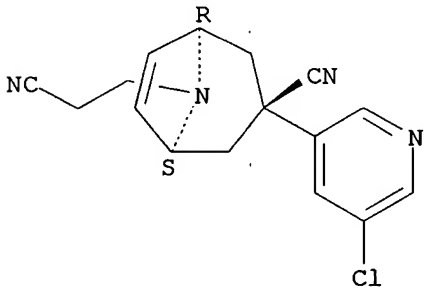
Relative stereochemistry.




RN 209054-36-4 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-6-ene-8-propanenitrile, 3-(5-chloro-3-pyridinyl)-3-cyano-, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.




REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:330897 CAPLUS

DOCUMENT NUMBER: 127:44445

TITLE: The SAR of UK-78,282: a novel blocker of human T cell Kv1.3 potassium channels

AUTHOR(S): Burgess, Laurence E.; Koch, Kevin; Cooper, Kelvin; Biggers, Michael S.; Ramchandani, Mukesh; Smitrovich, Jacqueline H.; Gilbert, Eric J.; Bruns, Matthew J.; Mather, Robert J.; et al.

CORPORATE SOURCE: Central Research Division, Department of Medicinal Chemistry, Pfizer Inc., Groton, CT, 06340, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(8), 1047-1052
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

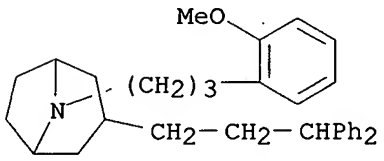
AB UK-78,282 was identified in a human T cell 86Rb efflux high-throughput screen of our compound libraries. This compound was found to be a potent and

selective blocker of human T cell voltage-gated K+ channels and to inhibit T cell activation. The SAR around UK-78,282 and a general pharmacophore hypothesis are presented in this communication.

IT 191217-58-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(structure-activity relationships of synthetic derivs. of UK-78,282 T-cell Kv1.3 potassium channel blocker)

RN 191217-58-0 CAPLUS

CN 8-Azabicyclo[3.2.1]octane, 3-(3,3-diphenylpropyl)-8-[3-(2-methoxyphenyl)propyl]- (9CI) (CA INDEX NAME)




REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

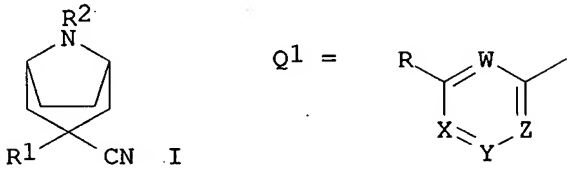
L4 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:101571 CAPLUS
DOCUMENT NUMBER: 126:104021
TITLE: Preparation of 3-aryl-3-cyano-8-azabicyclo[3.2.1]octanes as insecticides and acaricides.
INVENTOR(S): Urch, Christopher John; Salmon, Roger; Lewis, Terence; Godfrey, Christopher Richard Ayles; Clough, Martin Stephen
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9637494 | A1 | 19961128 | WO 1996-GB1151 | 19960513 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN | | | | |
| CA 2217064 | A1 | 19961128 | CA 1996-2217064 | 19960513 |
| AU 9656988 | A | 19961211 | AU 1996-56988 | 19960513 |
| AU 710540 | B2 | 19990923 | | |
| EP 828739 | A1 | 19980318 | EP 1996-915100 | 19960513 |
| EP 828739 | B1 | 20020911 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| CN 1185154 | A | 19980617 | CN 1996-194135 | 19960513 |
| CN 1066730 | B | 20010606 | | |
| GB 2324795 | A | 19981104 | GB 1998-16362 | 19960513 |
| GB 2324795 | B | 19990519 | | |
| HU 9802708 | A2 | 19990201 | HU 1998-2708 | 19960513 |
| BR 9609112 | A | 19990202 | BR 1996-9112 | 19960513 |

| | | | | | |
|---|---|---|---|---|---|
| JP 11505826 | T | 19990525 | JP 1996-535466 | | 19960513 |
| AP 803 | A | 20000124 | AP 1997-1139 | | 19960513 |
| W: GH, KE, LS, MW, SD, SZ, UG, ZW | | | | | |
| AT 223913 | T | 20020915 | AT 1996-915100 | | 19960513 |
| PT 828739 | T | 20021231 | PT 1996-915100 | | 19960513 |
| ES 2183950 | T3 | 20030401 | ES 1996-915100 | | 19960513 |
| IL 118254 | A | 20020421 | IL 1996-118254 | | 19960514 |
| IL 127075 | A | 20030212 | IL 1996-127075 | | 19960514 |
| ZA 9603875 | A | 19961202 | ZA 1996-3875 | | 19960515 |
| IN 1996DE01041 | A | 20050311 | IN 1996-DE1041 | | 19960517 |
| US 5922732 | A | 19990713 | US 1996-651182 | | 19960524 |
| US 6207676 | B1 | 20010327 | US 1998-207195 | | 19981208 |
| AU 9936832 | A | 19990916 | AU 1999-36832 | | 19990629 |
| AU 720176 | B2 | 20000525 | | | |
| US 6391883 | B1 | 20020521 | US 2000-602711 | | 20000626 |
| US 6573275 | B1 | 20030603 | US 2002-124696 | | 20020412 |
| PRIORITY APPLN. INFO.: | | | GB 1995-10459 | A | 19950524 |
| | | | AU 1996-56988 | A3 | 19960513 |
| | | | GB 1996-9978 | A3 | 19960513 |
| | | | WO 1996-GB1151 | W | 19960513 |
| | | | IL 1996-118254 | A3 | 19960514 |
| | | | US 1996-651182 | A3 | 19960524 |
| | | | US 1998-207195 | A3 | 19981208 |
| | | | US 2000-602711 | A3 | 20000626 |

OTHER SOURCE(S): MARPAT 126:104021

GI



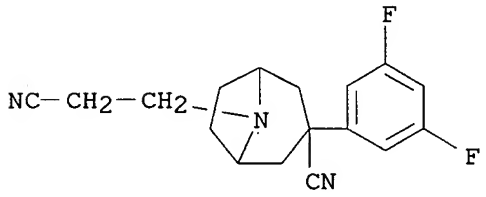

AB Title compds. [I; R1 = Q1; W, X, Y, Z = CR, N; provided that ≤2 of W, X, Y, Z = N; R = H, halo, cyano, amino, hydrazino, acylamino, OH, alkyl, hydroxyalkyl, alkoxy, haloalkyl, haloalkoxy, alkenyl, alkenyloxy, alkoxyalkenyl, alkynyl, carboxylic acyl, alkoxycarbonyl, aryl, heterocyclyl; R2 = H, cyano, (substituted) alkyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkenyl, aralkenyl, alkynyl, alkoxycarbonyl, alkanesulfonyl, arenesulfonyl, alkanyloxycarbonyl, aralkyloxycarbonyl, arloxycarbonyl, heterocyclyalkyl, carbamyl, dithiocarboxyl], were prepared Thus, tropinone and tosylmethyl isocyanide in dimethoxyethane/EtOH at 0° were treated with KOCMe3 and the mixture was stirred 4 h at room temperature to give exo-3-cyano-8-methyl-8-azabicyclo[3.2.1]octane. The latter in THF was added to LiN(CHMe2)2 in THF at -25° and the mixture was cooled to -78°; 3-fluoropyridine was added and the mixture was warmed to room temperature over 6 h to give exo-3-(3-pyridyl)-endo-3-cyano-8-methyl-8-azabicyclo[3.2.1]octane. The latter at 500 ppm was 80-100% effective against Myzus persicae.

IT 185982-37-0P 185982-51-8P 185982-87-0P
185982-89-2P 185983-07-7P 185983-58-8P
185983-59-9P 185983-78-2P 185983-97-5P
185984-13-8P 185984-31-0P 185984-47-8P
185984-58-1P 185985-20-0P 185985-21-1P
185985-24-4P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-aryl-3-cyano-8-azabicyclo[3.2.1]octanes as insecticides

and acaricides)

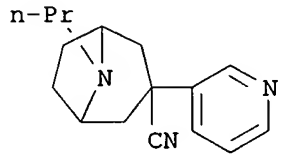
RN 185982-37-0 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-8-propanenitrile, 3-cyano-3-(3,5-difluorophenyl)- (9CI) (CA INDEX NAME)



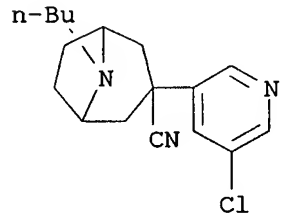

RN 185982-51-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-3-carbonitrile, 8-propyl-3-(3-pyridinyl)- (9CI) (CA INDEX NAME)



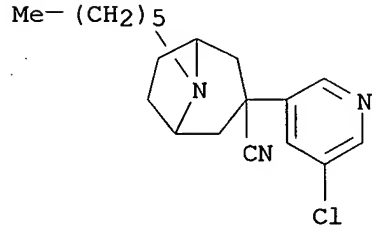

RN 185982-87-0 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-3-carbonitrile, 8-butyl-3-(5-chloro-3-pyridinyl)- (9CI) (CA INDEX NAME)



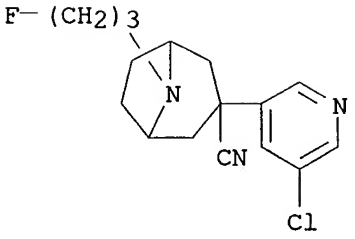

RN 185982-89-2 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-3-carbonitrile, 3-(5-chloro-3-pyridinyl)-8-hexyl- (9CI) (CA INDEX NAME)

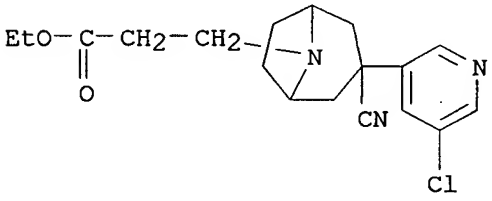



RN 185983-07-7 CAPLUS

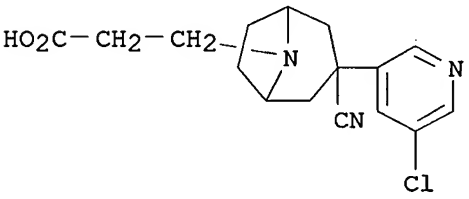
CN 8-Azabicyclo[3.2.1]octane-3-carbonitrile, 3-(5-chloro-3-pyridinyl)-8-(3-fluoropropyl)- (9CI) (CA INDEX NAME)



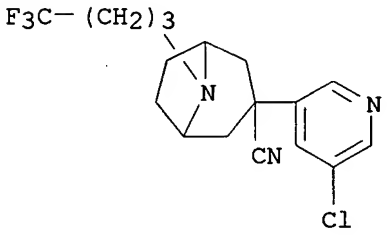
RN 185983-58-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-8-propanoic acid, 3-(5-chloro-3-pyridinyl)-3-cyano-, ethyl ester (9CI) (CA INDEX NAME)



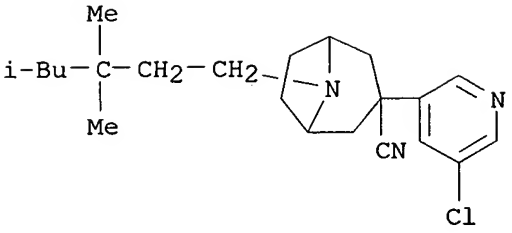
RN 185983-59-9 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-8-propanoic acid, 3-(5-chloro-3-pyridinyl)-3-cyano- (9CI) (CA INDEX NAME)



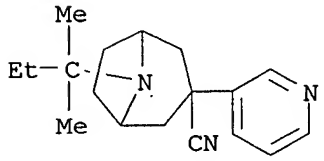
RN 185983-78-2 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carbonitrile, 3-(5-chloro-3-pyridinyl)-8-(4,4,4-trifluorobutyl)- (9CI) (CA INDEX NAME)



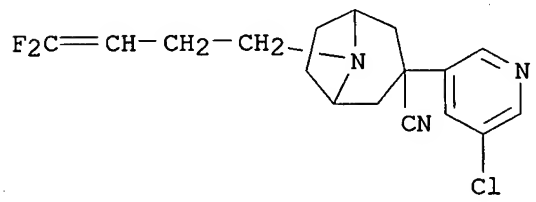
RN 185983-97-5 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carbonitrile, 3-(5-chloro-3-pyridinyl)-8-(3,3,5-trimethylhexyl)- (9CI) (CA INDEX NAME)



RN 185984-13-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carbonitrile, 8-(1,1-dimethylpropyl)-3-(3-pyridinyl)- (9CI) (CA INDEX NAME)

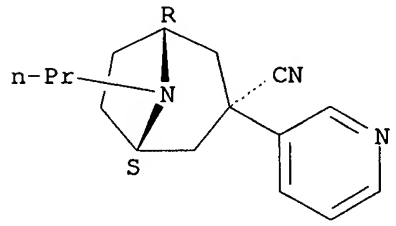


RN 185984-31-0 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carbonitrile, 3-(5-chloro-3-pyridinyl)-8-(4,4-difluoro-3-butenyl)- (9CI) (CA INDEX NAME)



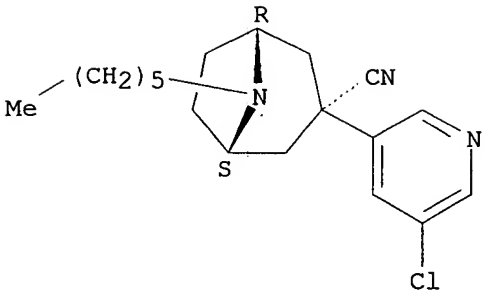
RN 185984-47-8 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carbonitrile, 8-propyl-3-(3-pyridinyl)-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



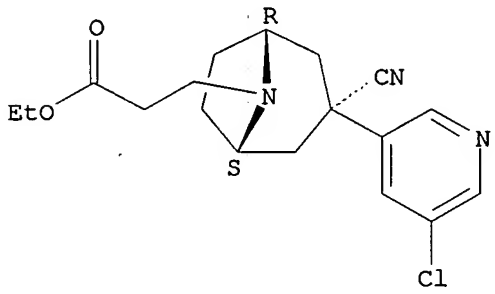
RN 185984-58-1 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carbonitrile, 3-(5-chloro-3-pyridinyl)-8-hexyl-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



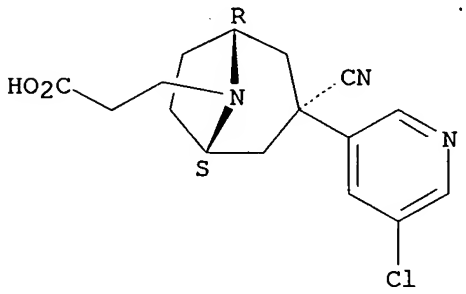

RN 185985-20-0 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-8-propanoic acid, 3-(5-chloro-3-pyridinyl)-3-cyano-, ethyl ester, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



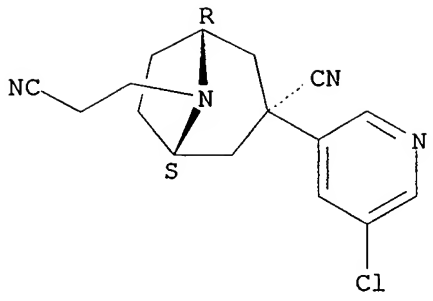

RN 185985-21-1 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-8-propanoic acid, 3-(5-chloro-3-pyridinyl)-3-cyano-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.




RN 185985-24-4 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-8-propanenitrile, 3-(5-chloro-3-pyridinyl)-3-cyano-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.

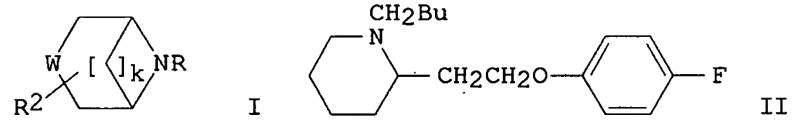



L4 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:106776 CAPLUS
DOCUMENT NUMBER: 120:106776
TITLE: Preparation of (phenoxyalkyl)piperidines and analogs as calcium channel antagonists
INVENTOR(S): Brown, Thomas Henry; Cooper, David Gwyn; King, Ronald Joseph; Orlek, Barry Sidney
PATENT ASSIGNEE(S): SmithKline Beckman Corp., UK
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9315052 | A1 | 19930805 | WO 1993-GB173 | 19930127 |
| W: AU, CA, JP, KR, NZ, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9333644 | A | 19930901 | AU 1993-33644 | 19930127 |
| EP 629190 | A1 | 19941221 | EP 1993-902469 | 19930127 |
| R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| JP 07503461 | T | 19950413 | JP 1993-513047 | 19930127 |

PRIORITY APPLN. INFO.:
GB 1992-1744 A 19920128
GB 1992-1745 A 19920128
GB 1992-1746 A 19920128
GB 1992-1752 A 19920128
WO 1993-GB173 A 19930127

OTHER SOURCE(S): MARPAT 120:106776
GI

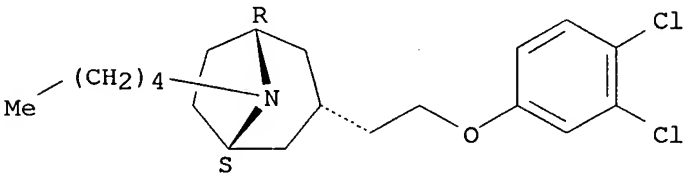



AB Title compds. [I; R = H (k = 2), (cyclo)alkyl, phenylalkyl, etc.; R2 = (CH2)nA(CH2)mR3; A = bond, CH:CH, O, NH, etc.; R3 = (hetero)aryl; W = bond, CH2, O, S; k = 0 or 2 when W = CH2; m, n = 0-6] were prepared Thus, 2-(2-hydroxyethyl)piperidine was N-alkylated by BuCH2Br and the product condensed with 4-FC6H4OH to give title compound II. I gave 30-100% inhibition of plateau Ca2+ current in rat dorsal root ganglion neurons at 20 μM in vitro.

IT 152009-16-0P 152601-96-2P
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as calcium channel antagonist)
RN 152009-16-0 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[2-(3,4-dichlorophenoxy)ethyl]-8-pentyl-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.

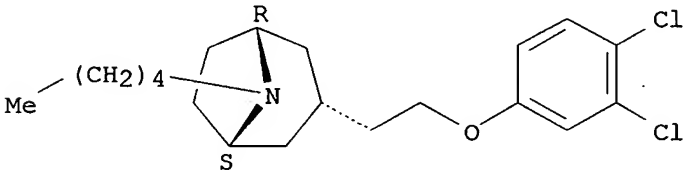



RN 152601-96-2 CAPLUS
CN 8-Azabicyclo[3.2.1]octane, 3-[2-(3,4-dichlorophenoxy)ethyl]-8-pentyl-, endo-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

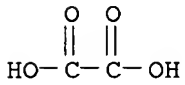
CRN 152009-16-0
CMF C20 H29 Cl2 N O

Relative stereochemistry.




CM 2

CRN 144-62-7
CMF C2 H2 O4




L4 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:93788 CAPLUS
DOCUMENT NUMBER: 118:93788
TITLE: Opioid properties of some derivatives of pethidine based on tropane
AUTHOR(S): Casy, A. F.; Dewar, G. H.; Pascoe, R. A.
CORPORATE SOURCE: Sch. Pharm. Pharmacol., Univ. Bath, Bath, BA2 7AY, UK
SOURCE: Journal of Pharmacy and Pharmacology (1992), 44(10), 787-90
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 118:93788
AB The preparation of some tropane analogs of pethidine and its reversed ester, chiefly with preferred 3α-m-hydroxyphenyl chair conformations, is described. The former were secured from tropan-3-one in a sequence of

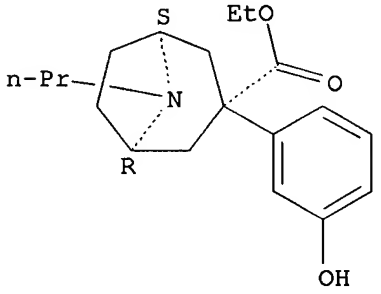
reactions involving cyanide attack, hydrolysis, Grignard attack and then rearrangements. The reversed ester was obtained by treating tropan-3-one with lithium Ph, followed by acylation. Configurational and conformational assignments follow from NMR anal. The antinociceptive potencies of these compds. in mice are reported, and discussed in relation to non-phenolic congeners and the 4-arylpiperidine moiety of morphine.

IT 145879-81-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and analgesic activity of)

RN 145879-81-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-3-carboxylic acid, 3-(3-hydroxyphenyl)-8-propyl-, ethyl ester, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.

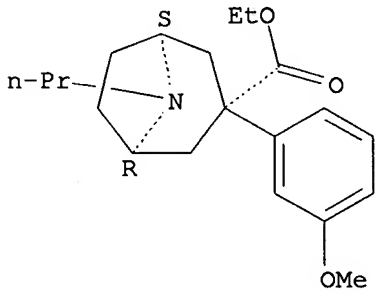



IT 145879-74-9P 145879-75-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 145879-74-9 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-3-carboxylic acid, 3-(3-methoxyphenyl)-8-propyl-, ethyl ester, hydrochloride, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.

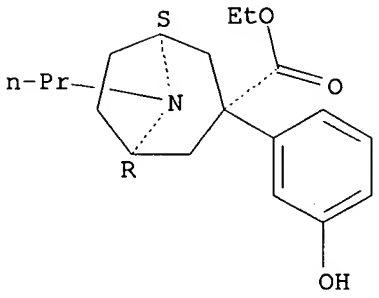



● HCl

RN 145879-75-0 CAPLUS

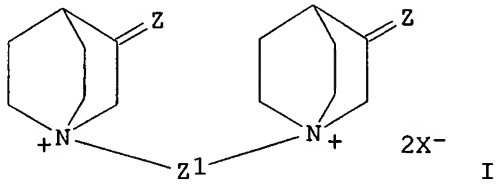
CN 8-Azabicyclo[3.2.1]octane-3-carboxylic acid, 3-(3-hydroxyphenyl)-8-propyl-, ethyl ester, hydrochloride, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.

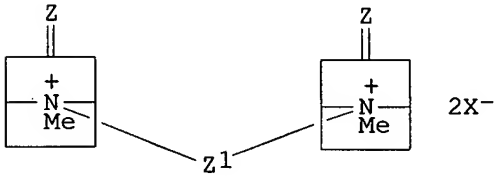



● HCl

L4 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:55866 CAPLUS
DOCUMENT NUMBER: 108:55866
TITLE: Synthesis and neuromuscular blocking activity of symmetrical bis- and poly-quaternary derivatives of quinuclidine and tropine
AUTHOR(S): Chen, Shengquan; Yu, Shongtao; Geng, Rongliang; Dan, Zhiyi
CORPORATE SOURCE: Inst. Basic Med. Sci., Acad. Mil. Med. Sci., Beijing, Peop. Rep. China
SOURCE: Yaoxue Xuebao (1987), 22(5), 347-53
CODEN: YHHPAL; ISSN: 0513-4870
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI




I




II

AB Title compds. e.g., I and II [Z = O, NOH; Z1 = (CH2)6, CH2OCH2; X = Br, Cl] were prepared from quinuclidine or tropine derivs. and their neuromuscular blocking activity was reported.

IT 112546-62-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and neuromuscular blocking activity of)

RN 112546-62-0 CAPLUS

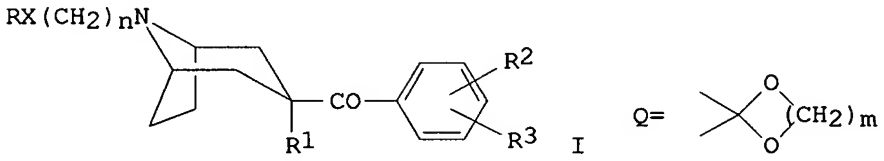
CN 8-Azoniabicyclo[3.2.1]octane, 8,8'-(1,6-hexanediyl)bis[3-(2-ethoxy-2-oxoethyl)-8-methyl-, dibromide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L4 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:161003 CAPLUS
DOCUMENT NUMBER: 98:161003
TITLE: Tropyl derivatives
INVENTOR(S): Tomesch, John C.
PATENT ASSIGNEE(S): Sandoz, Inc., USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

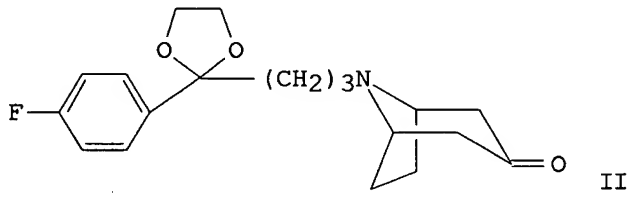
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 4366154 | A | 19821228 | US 1981-319254 | 19811109 |
| PRIORITY APPLN. INFO.: | | | US 1981-319254 | 19811109 |

OTHER SOURCE(S): CASREACT 98:161003; MARPAT 98:161003
GI




I



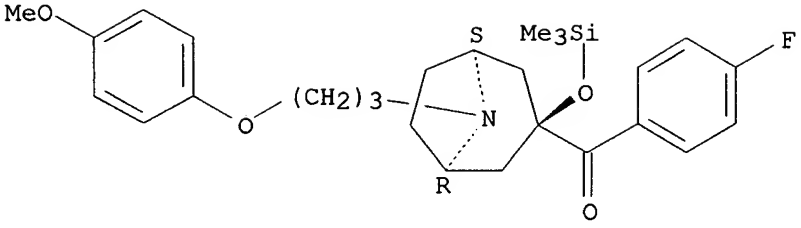

II

AB The neurotropic (no data) title compds. I [R = (un)substituted Ph, (un)substituted 10H-phenothiazin-10-yl; R1 = H, HO; R2, R3 = H, F, Cl, Br, C1-4 alkyl, C1-4 alkoxy, F3C; n = 1-4; X = CO, Q (m = 2, 3)] and their salts were prepared Thus, 2,6-cycloheptadienone cyclized with 2-(4-fluorophenyl)-1,3-dioxolane-2-propanamine to give the azabicyclooctanone II, which reacted with p-FC6H4CH(OEt)P(O)(OEt)2 followed by hydrolysis to give I (RX = p-FC6H4CO, R1 = R2 = H, R3 = p-F, n = 3).

IT 85329-99-3P 85330-00-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

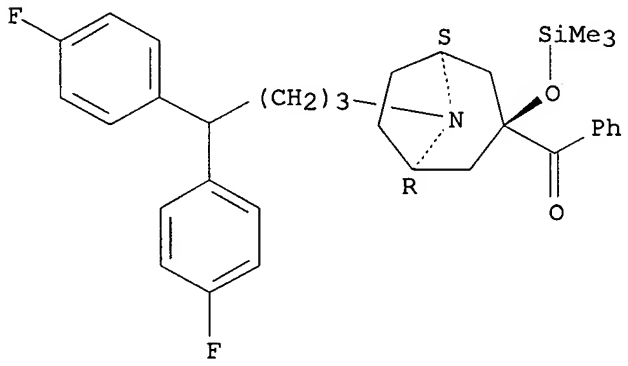
RN 85329-99-3 CAPLUS
CN Methanone, (4-fluorophenyl)[8-[3-(4-methoxyphenoxy)propyl]-3-[(trimethylsilyl)oxy]-8-azabicyclo[3.2.1]oct-3-yl]-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



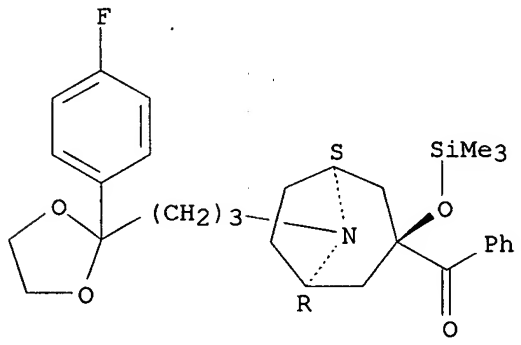
RN 85330-00-3 CAPLUS
CN Methanone, [8-[4,4-bis(4-fluorophenyl)butyl]-3-[(trimethylsilyl)oxy]-8-azabicyclo[3.2.1]oct-3-yl]phenyl-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



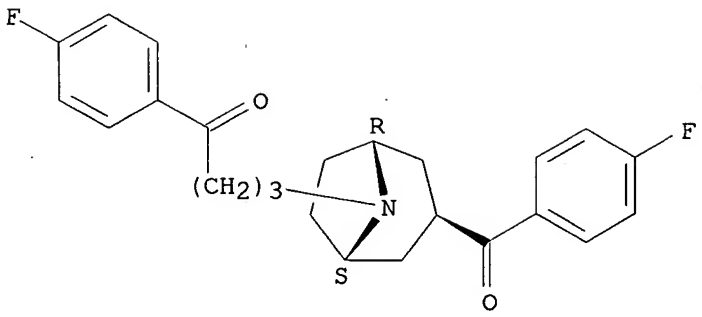
IT 85329-92-6P 85329-97-1P 85329-98-2P
85330-02-5P 85330-04-7P 85345-63-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 85329-92-6 CAPLUS
CN Methanone, [8-[3-[2-(4-fluorophenyl)-1,3-dioxolan-2-yl]propyl]-3-[(trimethylsilyl)oxy]-8-azabicyclo[3.2.1]oct-3-yl]phenyl-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



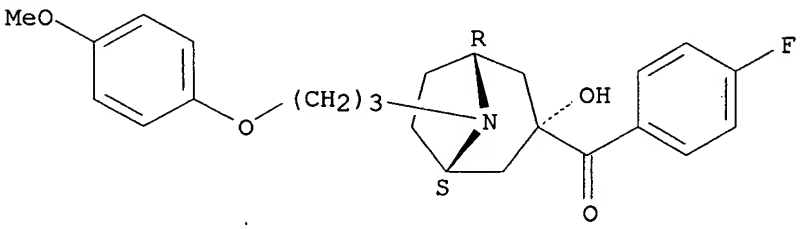
RN 85329-97-1 CAPLUS
CN 1-Butanone, 4-[3-(4-fluorobenzoyl)-8-azabicyclo[3.2.1]oct-8-yl]-1-(4-fluorophenyl)-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



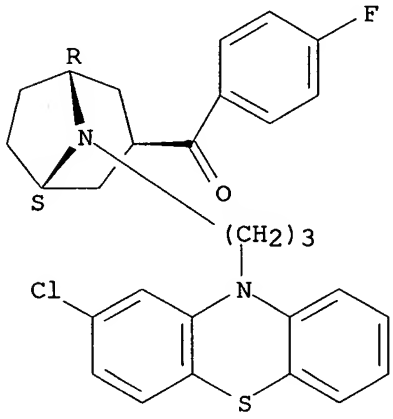
RN 85329-98-2 CAPLUS
CN Methanone, (4-fluorophenyl)[3-hydroxy-8-[3-(4-methoxyphenoxy)propyl]-8-azabicyclo[3.2.1]oct-3-yl]-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



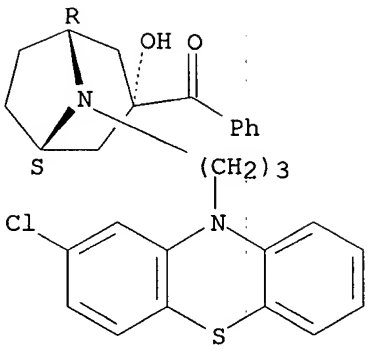
RN 85330-02-5 CAPLUS
CN Methanone, [8-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-8-azabicyclo[3.2.1]oct-3-yl](4-fluorophenyl)-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



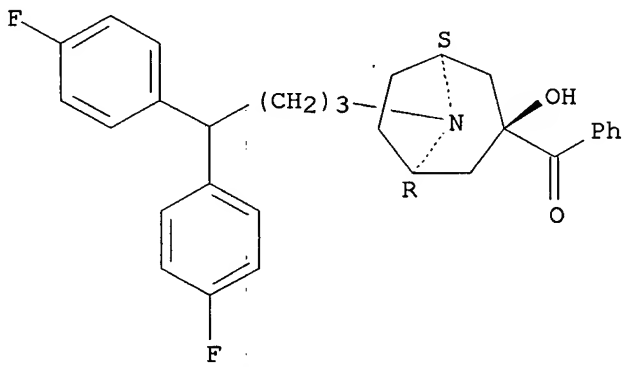
RN 85330-04-7 CAPLUS
CN Methanone, [8-[3-(2-chloro-10H-phenothiazin-10-yl)propyl]-3-hydroxy-8-azabicyclo[3.2.1]oct-3-yl]phenyl-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 85345-63-7 CAPLUS
CN Methanone, [8-[4,4-bis(4-fluorophenyl)butyl]-3-hydroxy-8-azabicyclo[3.2.1]oct-3-yl]phenyl-, endo- (9CI) (CA INDEX NAME)

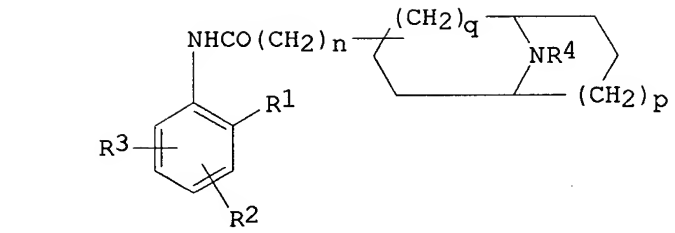
Relative stereochemistry.



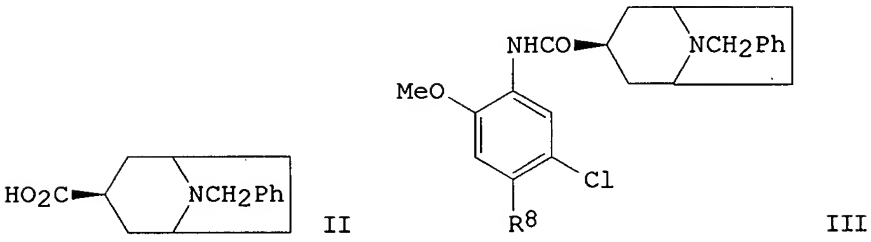
L4 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:6586 CAPLUS
DOCUMENT NUMBER: 96:6586
TITLE: Aniline derivatives
INVENTOR(S): Hadley, Michael Stewart; Blaney, Frank Edward
PATENT ASSIGNEE(S): Beecham Group Ltd. , UK
SOURCE: Eur. Pat. Appl., 98 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 31219 | A1 | 19810701 | EP 1980-304467 | 19801211 |
| EP 31219 | B1 | 19840307 | | |
| R: AT, BE, CH, DE, FR, GB, IT, NL, SE | | | | |
| US 4350691 | A | 19820921 | US 1980-213237 | 19801205 |
| ZA 8007691 | A | 19811125 | ZA 1980-7691 | 19801209 |
| DK 8005414 | A | 19810621 | DK 1980-5414 | 19801218 |
| AU 8065528 | A | 19810625 | AU 1980-65528 | 19801218 |
| JP 56092888 | A | 19810727 | JP 1980-180319 | 19801219 |
| ES 498013 | A1 | 19820401 | ES 1980-498013 | 19801219 |
| PRIORITY APPLN. INFO.: | | | GB 1979-43985 A | 19791220 |
| OTHER SOURCE(S): | MARPAT 96:6586 | | | |

GI



I



II III

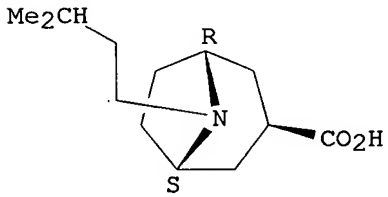
AB Carboxamilides I [R1 = C1-6 alkoxy or alkylthio; R2, R3 independently = H, halo, CF3, C1-7 acyl or acylamino, NH2, N2NCO, or H2NSO2 optionally substituted (o.s.) by 1 or 2 C1-6 alkyl, alkylsulfonyl, sulfinyl, thio, or alkoxy, OH, NO2; R1R2 = OCH2O, OCH2CH2O; R4 = C1-7 alkyl, (CH2)sR6 [s = 0-2, R6 = C3-8 cycloalkyl, (CH2)t R7 (t = 1, 2, R7 = Ph o.s. by 1 or 2 C1-6 alkyl, C1-4 alkoxy, CF3, halo, thienyl)], n, p, q independently = 0-2], useful as antiemetics, central nervous depressants, and gastric motility promoters, were prepared 8-Benzylnortropan-3-one was converted in 2 steps to bicyclic acid II which was successively amidated to amide III (R8 = H), nitrated to III (R8 = NO2), hydrogenated to amine III (R8 = NH2), and N-acylated to III (R8 = AcNH). III (R8 = NH2) had depressant ED50 0.05 mg/kg (mouse climbing test); 1 mg/kg gave 100% inhibition of climbing.

IT 79522-04-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, by aminochloroanizole)

RN 79522-04-6 CAPLUS

CN 8-Azabicyclo[3.2.1]octane-3-carboxylic acid, 8-(3-methylbutyl)-, hydrochloride, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.

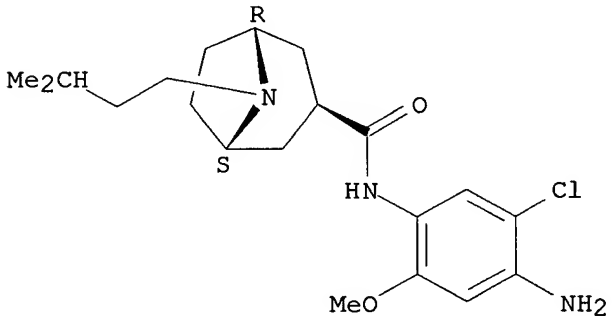


● HCl

IT 79522-25-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and depressant activity of)

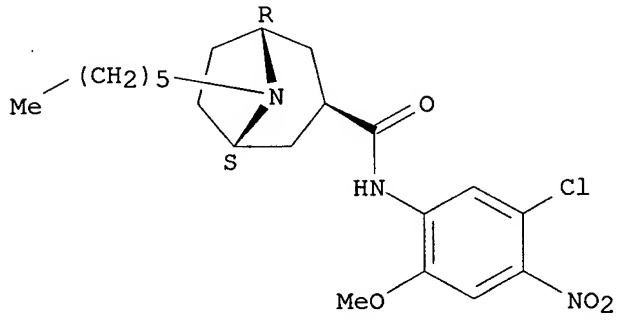
RN 79522-25-1 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carboxamide, N-(4-amino-5-chloro-2-methoxyphenyl)-8-(3-methylbutyl)-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



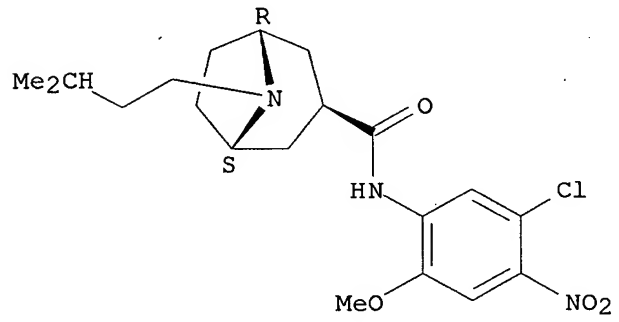

IT 79522-16-0P 79522-17-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)
RN 79522-16-0 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carboxamide, N-(5-chloro-2-methoxy-4-nitrophenyl)-8-hexyl-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.




RN 79522-17-1 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carboxamide, N-(5-chloro-2-methoxy-4-nitrophenyl)-8-(3-methylbutyl)-, exo- (9CI) (CA INDEX NAME)

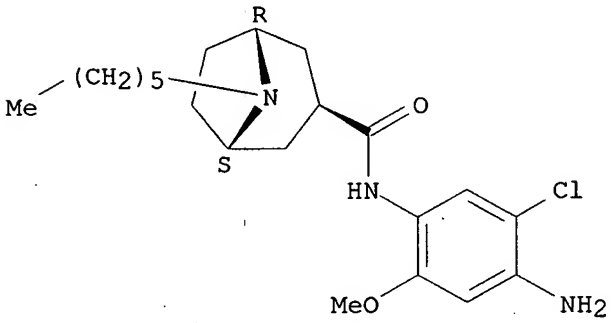
Relative stereochemistry.




IT 79522-24-0P
RL: SPN (Synthetic preparation); PREP (Preparation)

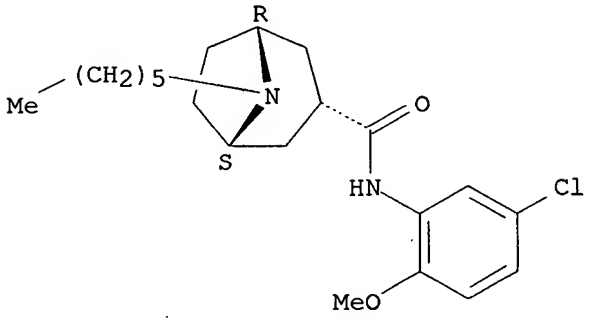
(preparation of)
RN 79522-24-0 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carboxamide, N-(4-amino-5-chloro-2-methoxyphenyl)-8-hexyl-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



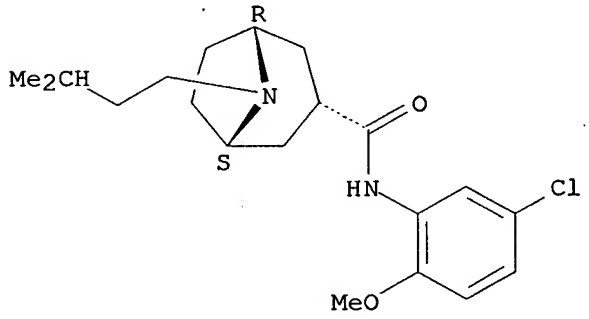
IT 79521-96-3 79521-97-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation by, of Me nortropanecarboxylate)
RN 79521-96-3 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carboxamide, N-(5-chloro-2-methoxyphenyl)-8-hexyl-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 79521-97-4 CAPLUS
CN 8-Azabicyclo[3.2.1]octane-3-carboxamide, N-(5-chloro-2-methoxyphenyl)-8-(3-methylbutyl)-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1964:75528 CAPLUS
DOCUMENT NUMBER: 60:75528
ORIGINAL REFERENCE NO.: 60:13285h,13286a-h,13287a-c
TITLE: 3-(Monocarbocyclic aryl)-3-carboxytropanes and esters thereof
INVENTOR(S): Archer, Sydney; Bell, Malcolm R.
PATENT ASSIGNEE(S): Sterling Drug Inc.
SOURCE: 14 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3120537 | | 19640204 | US 1958-731857 | 19580430 |
| PRIORITY APPLN. INFO.: | | | US | 19580430 |

GI For diagram(s), see printed CA Issue.

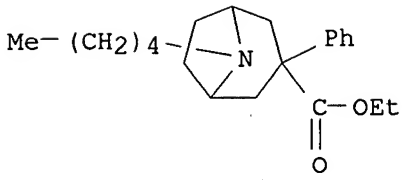
AB The title compds. (I, R1 = alkyl) are useful as analgesics. Thus, an aqueous solution of nortropinone hydrochloride and KCN, kept below 25°, formed the cyanohydrin which was hydrolyzed to the hydroxy acid (II, R = R1 = H) in concentrated, aqueous HCl. The acid, after refluxing 20 hrs. in MeOH-HCl, formed nor-α-ecgonine Me ester (II, R = H, R1 = Me), m. 144-7° (EtOAc). The ester, refluxed with PhCH2CH2Br and KOAc, formed 8-(2-phenylethyl)nor-α-ecgonine Me ester (II, R = PhCH2CH2, R1 = Me) which formed a hydrochloride, m. 223-9° (decomposition). Similarly, II Me esters (R1 = Me) were prepared (R given): propargyl; p-H2NC6H4CH2CH2; PhCH2; PhCH2CH2CH2; p-MeOC6H4CH2CH2; p-ClC6H4CH2CH2; cinnamyl (p-MeC6H4SO3H salt m. 201-2°). A solution of α-ecgonine Me ester (II, R = R1 = Me) in tetrahydrofuran (THF) was added to PhLi in Et2O over 20 min. and the mixt refluxed 1 hr. to give the carbinol (III, R = Me, R1 = R2 = Ph), m. 116-17° (hexane); hydrochloride m. 279.5-80.5° (decomposition). Similarly, III were prepared [R, R1, R2, salt, m.p. (decomposition) of the salt given]: Me, m-MeOC6H4, m-MeOC6H4, HCl, 236-7°; H, Ph, Ph, HCl.PrOH, 259.5°; PhCH2CH2, Ph, Ph, HCl, 271.5-4.0°; propargyl, Ph, Ph, --, --; p-H2NC6H4CH2CH2, Ph, Ph, --, --; PhCH2, Ph, Ph, --, --; PhCH2CH2CH2, Ph, Ph, --, --; p-MeOC6H4CH2CH2, Ph, Ph, --, --; p-ClC6H4CH2CH2, Ph, Ph, --, --. II (R = R1 = Me), and NaNH2 in liquid NH3 yielded 3-carbamoylpseudotropine, m. 155.8-9.2°, which, with EtMgBr in THF, formed 3-propionylpseudotropine (IV), m. 120.6-3.4°. IV and PhLi in THF formed III (CR = Me, R1 = Ph, R2 = Et), isolated as HCl salt, m. 212.4-13.8°. Thus, III was prepared (R, R1, R2, salt, m.p. of the salt given): Me, Et, m-MeOC6H4, HCl, 245.05.5° (decomposition). III (R = Me, R1 = R2 = Ph) with ZnCl2 in Ac2O at room temperature 80 min. formed V (β-series) (Va), m. 166.0-6.5° (Va.HCl m. 276-7°), while the same III, refluxed with Ac2O 20 hrs., formed V (α-series) (Vb), m. 162.0-45.° (Vb.HCl m. 265-6°). Vb heated with ZnCl2 in Ac2O on a steam bath 1.5 hrs. formed VI (α-series, R = Me, R1 = R2 = Ph), m. 312° (decomposition), while Va with ZnCl2 in Ac2O at room temperature 54 hrs. formed VI (β-series, R = Me, R1 = R2 = Ph), m. 121.0-2.5° (HCl salt m. 249-51°; MeI salt m. 233.5-7.5°). The latter was also formed from III (R = Me, R1 = R2 = Ph) and ZnCl2 in Ac2O at room temperature 63 hrs. Other III, with ZnCl2 in Ac2O at room temperature, formed the following VI (R, R1, R2, m.p., salt, m.p. of the salt given): Me, m-MeOC6H4, m-MeOC6H4 (VII), --, --, --; H, Ph, Ph (VIII), 209-12°, HCl, 290.0-1.5° (decomposition); PhCH2CH2, Ph, Ph, 112-14°, HCl, 266-7° (decomposition); propargyl, Ph, Ph, --, --, --; p-H2NC6H4CH2CH2, Ph, Ph, --, --, --; PhCH2, Ph, Ph, --, --, --; PhCH2CH2CH2, Ph, Ph, --, --, --; p-MeO-C6H4CH2CH2, Ph, Ph, --, --, --; p-ClC6H4CH2CH2, Ph, Ph, --, --, --; Me, Et, Ph, --, HCl, 273.2-5.8°; Me, Et, m-MeO-C6H4, --, HCl, 237.5-8.5°. VII

was demethylated with aqueous HBr to form the corresponding VI (R = Me, R1 = R2 = m-HO-C6H4). VI and H2NOH.HCl in pyridine and an alc. formed the oxime (IX). Thus, the following IX were prepared (R, R1, R2, m.p., salt, m.p. of the salt given): Me, Ph, Ph, --, HCl (β-series), 327° (decomposition); Me, Ph, Ph, --, -- (α-series), --; Me, p-MeOC6H4, p MeOC6H4, --, HCl, 295° (decomposition); PhCH2CH2, Ph, Ph, --, HCl, 313-15°; propargyl, Ph, Ph, --, --, --; p-H2NC6H4CH2CH2, Ph, Ph, --, --, --; PhCH2, Ph, Ph, --, --, --; PhCH2CH2CH2, Ph, Ph, --, --, --; p-MeOC6H4CH2CH2, Ph, Ph, --, --, --; p-ClC6H4CH2CH2, Ph, Ph, --, --, --; Me, Et, Ph (XI), --, --, --; Me, Et, m-MeOC6H4 (XII), --, --, --. IX heated on a steam bath with HOAc and HCl .apprx.2 hrs. formed I (R1 = H) which was esterified by standing at room temperature in the appropriate R1OH 15 hrs. to several days. Thus, the following I were prepared (R, R1, R2, m.p., salt, m.p. of the salt given): Me, Et, Ph (XIII), 187-91°, MeBr (β-series), 206.0-7.5°; Me, H, Ph (XIV), --, HCl (β-series), 224-5°; Me, Me, Ph, --, -- (β-series), --; Me, iso-Pr, Ph, --, -- (β-series), --; Me, Pr, Ph, --, -- (β-series), --; Me, Bu, Ph, --,(β-series), --; Me, n-hexyl, Ph, --, -- (β-series), --; Me, H, Ph, --, -- (α-series), --; Me, Et, Ph, --, -- (α-series), --; Me, H, m-HOC6H4, --, --, --; Me, Et, m-HOC6H4, --, --, --; Me, H, m-MeOC6H4 (XV), 235° (decomposition), HCl, 215.0-17.5°1; Me, Et, m-MeOC6H4, --, HBr, 178-80°; H, H, Ph (XVI), --, HCl, 275.0-6.5° (decomposition); H, Et, Ph (XVII), --, HCl, 219.521.5° (decomposition); PhCH2CH2, H, Ph, --, HCl, 224.0-4.5°; PhCH2-CH2, Et, Ph, --, HCl, 198.0-9.5°; propargyl, H, Ph, --, --, --; p-H2NC6H4CH2CH2, H, Ph, --, --, --; PhCH2, H, Ph, --, --, --; PhCH2CH2CH2, H, Ph, --, --, --; p-MeOC6H4CH2CH2, H, Ph, --, --, --; p-ClC6H4CH2CH2, H, Ph, --, --, --. Similarly, XI yielded XIV while XII yielded XV. XVI and SOCl2 formed the acid chloride which, with EtOH, formed XVII. XV was demethylated with aqueous HBr to the phenol (XVIII) which formed an HCl salt, m. 274.2-5.8°. XVIII in EtOH-HCl formed the Et ester (XIX) which, with acid chlorides or acid anhydrides, formed the corresponding Ph ester (XX). Thus, the XX were prepared (R given): Me, C5H11, HO2CCH2CH2, β-cyclopentylpropyl, Ph, PhCH2, 3,4,5 (MeO)3C6H2. XVII refluxed 17 hrs. with RBr and Na2CO3 in BuOH formed the corresponding I. Thus, I (R1 = Me, R2 = Ph) were prepared (R, salt, m.p. of the salt given): allyl, HCl, 193.5-4.0° (decomposition); cinnamyl, MeSO3H, 178.0-80.5°; PhNHCH2CH2, p-MeC6H4SO3H, 194-5°; n-C8H17, HCl, 138.8-46.0°; n-C5H11, HCl, 148.6-55.4°; propargyl, --, --; p-H2NC6H4CH2CH2, --, --; PhCH2, --, --; PhCH2CH2CH2, --, --; p-MeOC6H4CH2CH2, --, --; p-ClC6H4CH2CH2, --, --; cyclopropyl, --, --; cyclopropylmethyl, --, --; Et, --, --; PH2C(CN)CH2CH2, --, --. VI (R = Me, R1 = R2 = Ph, β-series), when reduced with LiAlH4 in refluxing Et2O 6 hrs., formed the corresponding carbinol (XXI), m. 160-1° (MeI salt m. 280.0-2.5°). VI in EtOH was also hydrogenated over PtO2 to XXI. VIII, when heated 5 hrs. with CNBr in benzene at 50-5° formed the corresponding N-cyano derivative, m. 160.5-2.5° which was reconverted to VIII by hydrolysis with aqueous HCl. Certain of the intermediates (I, R1 = H III V VI IX XXI) for the preparation of the title compds. are useful as anticholinergic or ganglionicblocking agents.

IT 95007-06-0P, 3-Nortropanecarboxylic acid, 8-pentyl-3-phenyl-, ethyl ester, hydrochloride 95749-73-8P, 3-Nortropanecarboxylic acid, 8-octyl-3-phenyl-, ethyl ester, hydrochloride
RL: PREP (Preparation)
(preparation of)

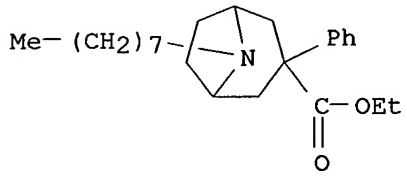
RN 95007-06-0 CAPLUS

CN 3-Nortropanecarboxylic acid, 8-pentyl-3-phenyl-, ethyl ester, hydrochloride (7CI) (CA INDEX NAME)



● HCl

RN 95749-73-8 CAPLUS
CN 3-Nortropanecarboxylic acid, 8-octyl-3-phenyl-, ethyl ester, hydrochloride (7CI) (CA INDEX NAME)



● HCl

L4 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1963:73513 CAPLUS
DOCUMENT NUMBER: 58:73513
ORIGINAL REFERENCE NO.: 58:12613f-h,12614a-e
TITLE: 3-Hydroxy-3-[(monocarbocyclic aryl)hydroxymethyl]tropanes
INVENTOR(S): Archer, Sydney; Bell, Malcolm
PATENT ASSIGNEE(S): Sterling Drug Inc.
SOURCE: 14 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3073829 | | 19630115 | US | 19600108 |
| PRIORITY APPLN. INFO.: | | | US | 19600108 |

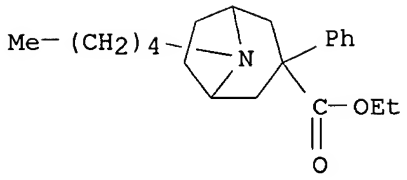
GI For diagram(s), see printed CA Issue.
AB Cf. the following abstract The compds. prepared have analgetic activity. A solution of 100 g. α-ecgonine Me ester in 325 ml. tetrahydrofuran was added during 20 min. to a stirred solution of PhLi (prepare from 316 g. PhBr and 27.9 g. Li wire) in 1 l. Et2O (vigorous reflux), the mixture stirred and refluxed 1 hr., then cooled and treated with 300 ml. H2O, the solid filtered off, washed with Et2O, the dark red filtrates decolorized with active C, dried (Na2SO4), treated with excess alc. HCl, and the precipitate filtered off and dried at 60° in vacuo 15 hrs. to give 167 g. I, HCl salt m. 279.5-80.5° (decomposition) (MeOH-Et2O). A sample of I was treated with aqueous Na2CO3 to give the free base, m. 116-17° (hexane). Fused, powdered ZnCl2 (10 g.) was added all at once to a stirred suspension of 10 g. I in 25 ml. (MeCO)2O at room temperature, the mixture which became homogeneous after 50 min., stirred 80 min. poured into a solution of 25 g.

NaOH in 200 ml. H2O, the tan solid collected, dried, extracted with 250 ml. boiling Me(CH2)4Me, concentrated to 100 ml., this cooled, and filtered to give 4.7 g. crystalline powder, m. 155-60°; the filtrate was concentrated to give an addnl. 1 g. The 2 crops were combined and recrystd. from 30 ml. boiling MeOH to give 4.3 g. 3-benzhydrylidenetropane epoxide (II), plates, m. 166-6.5°; HCl salt m. 276-7° (decomposition) (MeOH-Et2O). The ultraviolet spectrum of II showed ε 13,400, λ 220 mμ, and weak absorption peaks at 250-60 mμ. Similarly prepared were the following compds. (m.p. given): 3-phenyl-3-benzoyltropane, 121-2.5° (hexane), HCl salt 249-51° (absolute alc.), methiodide m. 233.5-7.5°; 3 - phenyl - 3 - (phenylisonitrosomethyl)tropane-HCl, 327° (decomposition); 3-phenyl-3-carboxytropane-HCl, 224-5° (decomposition) (MeOH-Et2O); 3-phenyl-3-carbethoxytropane-HCl, 187-91° (decomposition), methobromide, 206-7° (iso-PrOH-Et2O); 3-[di(m-anisyl)hydroxymethyl]pseudotropine, 236-7° (decomposition) (iso-PrOH-Et2O); 3-(m-anisyl)-3-(m-anisoyl)tropane showed a strong peak at 6.02 mμ; 3-(m-anisyl)-3-[(m-anisyl)isonitrosomethyl]-tropane-HCl, 295° (decomposition) (H2O); 3-(m-anisyl)-3-carboxytropane-HCl, 215-17.5° (PrOH-Et2O); 3-(m-anisyl)-3-carbethoxytropane-HBr, 178-80° (alc.-Et2O); nor-α-ecgonine Me ester, 144-7° (AcOEt); 3-(diphenylhydroxymethyl)(norpseudotropine-HCl), 259.5° (decomposition) (PrOH), it contains PrOH of crystallization; 3-phenyl-3-benzoylnortropane, 209-12° (PrOH); HCl salt 290-1.5° (decomposition) (PrOH-Et2O); 8-cyano-3-phenyl-3-benzoylnortropane, 160.5-2.5° (MeOH); 3-phenyl-3-(phenylisonitrosomethyl)nortropane-HCl, 286° (decomposition) (H2O); 3-phenyl-3-carbethoxynortropane-HCl, 219.5-21.5° (decomposition) (alc.-Et2O); 8-allyl-3-phenyl-3-carbethoxynortropane-HCl, 193.5-94° (decomposition) (iso-PrOH-Et2O); 8-cinnamyl-3-carbethoxy-3-phenylnortropane methanesulfonate, 178-80.5° (iso-PrOH-Et2O); 8-(2-phenylaminoethyl)-3-phenyl-3-carbethoxynortropane p-toluenesulfonate, 194-5° (PrOH); 8-(n-octyl)-3-phenyl-3-carbethoxynortropane-HCl, 38.8-46° (CCl4-Et2O); 8-(2-phenylethyl)nor-α-ecgonine Me ester-HCl, 223-9° (decomposition) (alc.-Et2O); 8-(2-phenylethyl)-3-(diphenylhydroxymethyl)norpseudotropine-HCl, 271.5-74° (decomposition) (MeOH-Et2O); 8-(2-phenylethyl)-3-phenyl-3-benzoylnortropane, 112-14° (hexane); HCl salt, 266-7° (decomposition) (absolute alc.); 8-(2-phenylethyl)-3-phenyl-3-(phenylisonitrosomethyl)nortropane-HCl, 313-15° (HCONMe2); 8-(2-phenylethyl)-3-phenyl-3-carboxynortropane-HCl, 224-4.5° (Me-OH-Et2O); 8-(2-phenylethyl)-3-phenyl-3-carbethoxynortropane-HCl, 198-9.5° (MeOH-Et2O); 8-cinnamylnor-α-ecgonine Me ester p-toluenesulfonate, 201-2° (iso-PrOH); 3-phenyl-3-(phenylhydroxymethyl)tropane, 160-1° (CCl4); methiodide, 280-2.5°; 3-carbamylpseudotropine, 155.8-9.2°; 3-propionylpseudotropine, 120.6-3.4° (hexane); 3-(ethylphenylhydroxymethyl)pseudotropine-HCl, 212.4-13.8° (MeOH-Et2O); 3-phenyl-3-propionyltropane-HCl, 273.2-5.8° (MeOH-Et2O); 3-[ethyl(m-anisyl)hydroxymethyl]pseudotropine - HCl, 245-5.5° (decomposition) (MeOH-Et2O); 3-(m-anisyl)-3-propionyltropane-HCl, 237.5-8.5° (iso-PrOH-Et2O); 3-(m-hydroxyphenyl)-3-propionyltropane-HCl, 274.2-5.8° (alc.-Et2O).

IT 95007-06-0P, 3-Nortropanecarboxylic acid, 8-pentyl-3-phenyl-, ethyl ester, hydrochloride 95749-73-8P, 3-Nortropanecarboxylic acid, 8-octyl-3-phenyl-, ethyl ester, hydrochloride
RL: PREP (Preparation)
(preparation of)

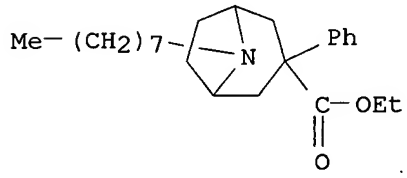
RN 95007-06-0 CAPLUS

CN 3-Nortropanecarboxylic acid, 8-pentyl-3-phenyl-, ethyl ester, hydrochloride (7CI) (CA INDEX NAME)



● HCl

RN 95749-73-8 CAPLUS
CN 3-Nortropanecarboxylic acid, 8-octyl-3-phenyl-, ethyl ester, hydrochloride (7CI) (CA INDEX NAME)



● HCl

L4 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1958:93024 CAPLUS
DOCUMENT NUMBER: 52:93024
ORIGINAL REFERENCE NO.: 52:16402b-f
TITLE: 8-Alkylnortropane derivatives
INVENTOR(S): Zirkle, Charles L.
PATENT ASSIGNEE(S): Smith, Kline & French Laboratories
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2800482 | | 19570723 | US 1955-519650 | 19550701 |

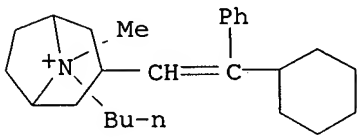
AB 3-Benzhydrylidenetropane picrate m. 237-8° (aqueous alc.); methobromide, m. 281-5° (iso-PrOH-Me2CO); etho(ethyl sulfate), white solid. Di(2-thienyl)-3-tropanylcarbinol (0.5 g.) in CHCl3 treated with dry HCl until strongly acid gave 2-[di(2-thienyl)methylidene]tropane-HCl, m. 224-5° (alc. Et2O). 1,1-Di(2-thienyl)-3-tropaneethanol (1 g.), 2 g. (CO2H)2, and 3 ml. H2O refluxed 2 hrs. gave 1,1-di(2-thienyl)-2-(3-tropanyl)ethylene, m. 74-6° (ligroine); picrate, m. 190-2° (aqueous Me2CO); HCl salt, m. 230-2° (alc. Et2O); methobromide, m. 252-3°. 1,1-Diphenyl-2-(3-tropanyl)ethylene methobromide, m. 286° (alc.); maleate; metho-p-toluene-sulfonate, white solid. 1-Phenyl-1-(2-thienyl)-3-tropaneethanol (9.7 g.), 19.4 g. (CO2H)2, and 29 ml. H2O refluxed 2 hrs. and the mixture made alkaline gave 1-phenyl-1-(2-thienyl)-2-(3-tropanyl)ethylene, m. 69-72°; picrate, m. 209-10°; tartrate, m. 174-5° (alc.-Et2O); methobromide, m. 258-9° (alc.-Et2O). 1-Phenyl-1-(2-pyridyl)-2-(3-tropanyl) ethylene methobromide, m. 228-30° (alc.-Et2O); tartrate, m. 165-7° (alc.-Et2O). 1-(2-Cyclohexylethyl)-1-phenyl-3-

tropaneethanol (1 g.) in 10 ml. AcOH and 3 ml. 37% HCl refluxed 0.5 hr. gave the dehydration product, λ 235 mμ, log ε 3.58. 1-Cyclohexyl-1-phenyl-2-(3-tropanyl) ethylene-HI, m. 222.5-4.0°; methobromide, m. 250-3° (H2O); butiodide, white solid. 1,1-Diphenyl-3-tropanepropanol (15 g.) in 50 ml. 37% HCl 1.5 hrs. at 100° gave 1,1-diphenyl-3-(3-tropane-1-propene, m. 59-60°, b0.4 170-3°; citrate, m. 174°. 1-(2-Pyridyl-1-p-tolyl-4-(3-tropanyl)-1-butanol (0.5 g.) and 2 ml. 85% H2SO4 heated 15 min. at 155° gave 1-(2-pyridyl)-1-p-tolyl-4-(3-tropanyl)-1-butene. A similar dehydration of 1-cyclopentyl-1-phenyl-3-tropanebutanol with HCl gave the corresponding butene as the HCl salt; neutralization with NH4OH gave the free base as a yellow oil.

IT 124111-32-6P, 8-Butyl-3-(β-cyclohexylstyryl)tropanium iodide
RL: PREP (Preparation)
(preparation of)

RN 124111-32-6 CAPLUS

CN 8-Butyl-3-(β-cyclohexylstyryl)tropanium iodide (6CI) (CA INDEX NAME)




● $I^-$

L4 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1958:93023 CAPLUS
DOCUMENT NUMBER: 52:93023
ORIGINAL REFERENCE NO.: 52:16401g-i,16402a-b
TITLE: 8-Alkylnortropane derivatives
INVENTOR(S): Zirkle, Charles L.
PATENT ASSIGNEE(S): Smith, Kline & French Laboratories
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2800481 | | 19570723 | US 1955-519649 | 19550701 |

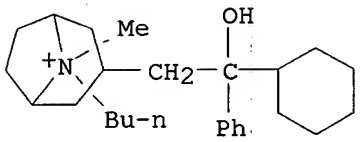
AB Me 3-tropanecarboxylate (10.1 g.) in 100 ml. Et2O stirred 1.5 hrs. at room temperature with PhLi gave diphenyl-3-tropanylcarbinol, m. 214-15° (aqueous MeOH); citrate, m. 112-18° (iso-PrOH-Et2O); methobromide, m. 309-10° (alc.). Et 3-tropaneacetate (I) (10 g.) in 20 ml. Et2O refluxed with PhLi and 11.8 g. thiophene in Et2O gave 1,1-di(2-thienyl 3-tropaneethanol, m. 138-40° (EtOAc); acetate, m. 189-90°; methobromide, m. 245.5° (alc.). 1,1-Diphenyl-3-tropaneethanol-HCl, m. 234-5° (alc.-Et2O); methobromide, m. 282-3° (alc.-Et2O). I with concentrated HCl gave 3-tropaneacetic acid-HCl (II), m. 172-4°. II (11 g.) refluxed with PhLi gave Ph 3-tropanylmethyl ketone (III), b0.2 138-41°. III (9 g.) stirred several hrs. at room temperature with PhLi gave 1,1-diphenyl-3-tropaneethanol-HBr, m. 230°. III (10 g.) treated with PhLi and thiophene gave 1-phenyl-1-(2-thienyl)-3-tropaneethanol, m. 137.5-9.0°; maleate, m. 145-6° (alc.-Et2O); methobromide, m. 256° (alc.). 1-Phenyl-1-(2-pyridyl)-3-tropaneethanol-HI, m. 194-6°; methobromide, m. 268°

(alc.). 1-Ethyl-1-phenyl-3-tropaneethanol-HCl, m. 237-7.5° (alc.). 1-Cyclohexyl-1-phenyl-3-tropaneethanol-HCl, m. 254-5° (alc.-Et2O); methobromide, m. 262° (alc.-Et2O). 2-Cyclohexylethyl 3-tropanylmethyl ketone picrate, m. 148-50°; 1-(2-cyclohexylethyl)-1-phenyl-3-tropaneethanol-HCl, m. 215-16°; citrate, m. 134-6° (Me2CO-MeOH); methobromide, m. 263-5°. II (3.7 g.) treated with SOCl2 gave the acid chloride HCl salt which treated with CH2N2 gave the diazomethyl 3-tropanylmethyl ketone and subsequent treatment with Ag2O oxide gave Et 3-tropanepropionate (IV). IV (18 g.) treated with PhLi as above gave 1,1-diphenyl-3-tropanepropanol, m. 141-2.5°; HCl salt, m. 249-50°; methobromide salt, m. 299°. Cyclopentyl 3-(3-tropanyl)propyl ketone (6.6 g.) treated with PhLi as above gave 1-cyclopentyl-1-phenyl-3-tropanebutanol. Diphenyl-3-tropanecarbinol etho(ethyl sulfate) was a white solid. 1,1-Diphenyl-3-tropaneethanol metho-p-toluenesulfonate, m. 172-4°; etho(ethyl sulfate), m. 234-5°; butobromide, m. 225-7°; butiodide, m. 227-9°. 1-Cyclohexyl-1-phenyl-2-(3-tropane)ethanol butyl bromide was a white solid.

IT 119640-59-4P, 8-Butyl-3-(β-cyclohexyl-β-hydroxyphenethyl)tropanium bromide
RL: PREP (Preparation)
(preparation of)

RN 119640-59-4 CAPLUS

CN 8-Butyl-3-(β-cyclohexyl-β-hydroxyphenethyl)tropanium bromide (6CI) (CA INDEX NAME)




● $Br^-$

L4 ANSWER 28 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1958:93020 CAPLUS
DOCUMENT NUMBER: 52:93020
ORIGINAL REFERENCE NO.: 52:16399b-i,16400a-i,16401a
TITLE: 8-Alkylnortropane derivatives
INVENTOR(S): Zirkle, Charles L.
PATENT ASSIGNEE(S): Smith, Kline & French Laboratories
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2800478 | | 19570723 | US 1955-519646 | 19550701 |

AB Some new physiologically active 3-substituted-8-alkylnortropanes, the nontoxic organic and inorg. salts, and the quaternary ammonium salts are described. Me 3-(3-hydroxytropane)carboxylate (10 g.) in 50 ml. Ac2O heated 4 hrs. at 100°, the excess Ac2O and AcOH removed in vacuo, the residue poured into H2O, extracted with Et2O, and the Et2O evaporated gave Me 3-(3-acetoxytropane)-carboxylate (I), m. 66-7°, b15 162-5°. I (29 g.) added dropwise during 7 min. to a vertical tube heated to

420° and filled with pieces of Pyrex tubing, the apparatus swept with N, the product dissolved in dilute HCl, extracted with Et2O, the aqueous acid solution saturated with K2CO3, and the product separated gave Me 3-(2-tropene)carboxylate (II), b15 131-4°, n25.5D 1.4998. II (13 g.) in 100 ml. MeOH hydrogenated over 5 g. Raney Ni at 50 lb./sq. in. at room temperature and the mixture distilled gave Me 3-tropanecarboxylate (III), b18 128-32°, n25D 1.4819. III (10.1 g.) in 100 ml. Et2O stirred 1.5 hrs. at room temperature with a solution of PhLi (from 34.5 g. PhBr and 3.5 g. Li) in 100 ml. Et2O, the mixture added to 150 ml. H2O, and the solid collected and purified gave diphenyl-3-tropanecarbinol (IV), m. 185.5-6.0° (EtOAc). IV (5.6 g.) in 20 ml. AcOH and 25 ml. dilute HCl refluxed 10 min. and evaporated to dryness gave 3-benzhydrylidenetropane-HCl, m. 275-8° (alc.-Et2O); free base (V), a colorless oil. V (4 g.) in alc. hydrogenated over Raney Ni at 400 lb./sq. in. at 60° and the product chromatographed on Al2O3 gave 3-benzhydryltropane (VI), m. 70-2°. VI (1 g.) gave the HCl salt, unmelted below 310°; MeBr salt, m. 277-9°; etho(ethyl sulfate), white solid. Tropinone (13.9 g.), 11.3 g. NCCH2CO2Et, 1.6 g. NH4OAc, 7.3 g. AcOH, 20 ml. alc., and 0.6 g. Pd-C shaken under H at 50° and 60 lb./sq. in. gave Et α-cyano-3-tropaneacetate (VII), b0.3 116-18°, n24D 1.4942. VII (8 g.) in 30 ml. 37% HCl refluxed 13 hrs. and the crude 3-tropaneacetic acid-HCl esterified by leaving 3 days at room temperature in 50 ml. alc. with dry HCl gave Et 3-tropaneacetate (VIII), b2 104-5°, n25D 1.4774. VIII (42 g.) in 100 ml. Et2O similarly treated with PhLi gave 1,1-diphenyl-3-tropaneethanol (IX), m. 146.5-7.5° (EtOAc). IX (14.6 g.) in 29 ml. 37% HCl and 100 ml. AcOH refluxed 0.5 hr. gave 1,1-diphenyl-2-(3-tropanyl)ethylene (X), as the HCl salt, m. 217-18° (alc.-Et2O); free X, m. 109.5-10.0° (Me2CO). X (10 g.) in alc. hydrogenated over Raney Ni at 500 lb./sq. in. and 60° gave 1,1-diphenyl-2-(3-tropanyl)ethane, colorless oil; HCl salt, m. 244-5°; methobromide, m. 257-8° (alc.-Et2O); metho-p-toluenesulfonate, white solid; maleate, obtained by treating with maleic acid in alc. VIII in 37% HCl refluxed several hrs. gave 3-tropaneacetic acid-HCl (XI), m. 172-4° (MeOH-Et2O). XI (11 g.) similarly treated with PhLi followed by passage of HCl gave the HCl salt which when washed was reconverted to phenyl 3-tropanylmethyl ketone (XII), b0.2 138-41°. BuLi (from 3.7 g. BuCl and 0.7 g. Li) in 25 ml. Et2O treated slowly at -45° with 5.5 g. 2-bromopyridine in 10 ml. Et2O, the mixture stirred 10 min., and 2.5 g. XII in 30 ml. Et2O added slowly, the mixture stirred 15 min. at -15°, 50 ml. H2O added, the mixture stirred a further 15 min., a solid collected, the solid stirred with CHCl3 and H2O, and the CHCl3 layer removed, combined with the Et2O layer and evaporated gave 1-phenyl-1-(2-pyridyl)-3-tropaneethanol (XIII), m. 117-18.5° (EtOAc). XIII (1 g.) and 2 ml. 85% H2SO4 heated 15 min. at 155° and the solution made basic gave 1-phenyl-1-(2-pyridyl)-2-(3-tropanyl)ethylene (XIV), m. 97.5-9.5° (Me2CO). XIV 0.2 g.), 5 g. cyclohexene, and 0.3 g. 20% Pd-C refluxed 48 hrs. gave 1-phenyl-1-(2-pyridyl)-2-(3-tropanyl)ethane (XV) as a thick oil; picrate, m. 201-3° (aqueous Me2CO). XV also forms the tartrate, m. 78-80° (alc.-Et2O). XII (12.2 g.) in 50 ml. Et2O added slowly to EtMgBr solution (from 7.3 g. Mg) at 0°, the mixture stirred 1.5 hrs. at room temperature, then refluxed 1.5 hrs., decomposed with ice and 21 g. NH4Cl in 50 ml. H2O, the Et2O layer removed, and the aqueous phase extracted with CHCl3 gave 1-ethyl-1-phenyl-3-tropaneethanol (XVI), m. 119-20°. XVI (0.44 g.) was dehydrated by heating 40 min. at 100° with 3 ml. concentrated HCl to the ethylene, m. 170-200°. The ethylene hydrogenated in alc. over Raney Ni at 60° and 500 lb./sq. in. gave 1-ethyl-1-phenyl-2-(3-tropanyl)ethane (XVII), an oil, which formed an HCl salt. VIII (15 g.) similarly treated with 2-cyclohexylethylmagnesium

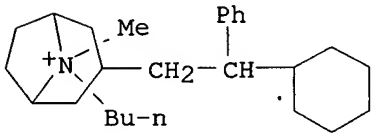
bromide gave 2-cyclohexylethyl 3-tropanylmethyl ketone (XVIII), b0.7 157-64°, n24.5D 1.5010. XVIII (7.7 g.) in 20 ml. Et2O similarly treated with PhLi (from 9.5 g. PhBr) in Et2O at 0° gave 1-(2-cyclohexylethyl)-1-phenyl-3-tropaneethanol (XIX), m. 104-6° (EtOAc). XIX (0.5 g.), 1 ml. HI, 3 ml. AcOH, and 0.13 g. red P refluxed 3.5 hrs., the solution filtered, the filtrate diluted with H2O, the crude HI salt separated as an oil and crystallized gave 1-(2-cyclohexylethyl)-1-phenyl-2-(3-tropanyl)ethane-HI, m. 175° (alc.-Et2O). The free base was a colorless oil; HCl salt, m. 198-200°. Similarly, 25 g. VIII reacted with cyclohexylmagnesium bromide to give cyclohexyl 3-tropanylmethyl ketone (XX), b0.9-1.1 142-53°, crystallizing to a white solid on standing. XX (10 g.) similarly treated with PhLi gave 1-cyclohexyl-1-phenyl-3-tropaneethanol (XXI), m. 139-40.5° (EtOAc). XXI (1 g.) refluxed 0.5 hr. with AcOH and concentrated HCl gave the ethylene HCl salt, m. 195-6°. Hydrolysis gave the free base as an oil. The free base (4.4 g.) hydrogenated over Raney Ni at 500 lb./sq. in. and 60° gave 1-cyclohexyl-1-phenyl-2-(3 tropanyl)ethane, colorless oil; HCl salt, m. 167-8.5°; citrate, m. 153-5°; butiodide, white solid. N-Isopropylnortropanone (16.7 g.), 11.3 g. NCCH2CO2Et, 1.6 g. NH4OAc, 7.3 g. AcOH, 20 ml. alc., and 0.6 g. Pd-C shaken with H at 60 lb./sq. in. and 60°, the residue refluxed 12 hrs. with concentrated HCl gave crude 3-(N-isopropylnortropane)-acetic acid-HCl which was esterified with anhydrous MeOH and HCl 3 days at room temperature gave Me 3-(N-isopropylnortropane)acetate (XXII), b0.3 124-7°. XXII (11.3 g.) similarly treated with p-anisylmagnesium bromide gave p-anisyl 3-(N-isopropylnortropanyl)methyl ketone (XXIII), b0.2 160-4° and crystallized as a white solid. XXIII (7.5 g.) similarly treated with PhLi at 0° gave 1-(p-anisyl)-1-phenyl-3-(N-isopropylnortropane)ethanol (XXIV), white solid. Dehydration of XXIV with oxalic acid and H2O gave the ethylene, which when hydrogenated as described above gave 1-p-anisyl-1-phenyl-2-[3-(N-isopropylnortropanyl)]ethane; methobromide salt. VIII (164 g.) in 500 ml. Et2O refluxed 3 hrs. with 30 g. LiAlH4 in 2 l. Et2O gave 3-tropaneethanol (XXV), m. 63-4° (C6H6-ligroine). XXV (10 g.) in 50 ml. CHCl3 treated with 14.3 g. SOCl2, refluxed 45 min., and isolation gave 1-chloro-2-(3-tropanyl)ethane-HCl, m. 167-8° (alc.-Et2O); free base, b0.9 81°. The base (47 g.) and 0.1 g. NaI refluxed 17 hrs. with 49 g. KCN in 175 ml. alc. and 75 ml. H2O, NaOH added to the residual mixture, and the product isolated gave 3-tropanepropionitrile (XXVI), b0.3 114-16°, n25D 1.4958. XXVI (25 g.) in 100 ml. 37% HCl refluxed several hrs., and evaporated, the residue dissolved in 300 ml. alc., 5 ml. concentrated H2SO4 added, and the residue treated with 40% NaOH gave Et 3-tropanepropionate (XXVII), b0.4 97-100°, n25D 1.4770. Similarly XXVII treated with PhLi gave 1,1-diphenyl-3-tropanepropanol (XXVIII), m. 141-2.5°. Dehydration of XXVII with concentrated HCl and 40% NaOH added gave 1,1-diphenyl-3-(3-tropanyl)-1-propene (XXIX), b0.4 170-3°, m. 59-60°. XXIX (4.7 g.) hydrogenated over 5 g. Raney Ni gave 1,1-diphenyl-3-(3-tropanyl)propane as an oil; citrate, m. 170°; methobromide, m. 277°. XXVII reduced with 3 g. LiAlH4 gave 3-tropanepropanol (XXX), b2 128-31°. XXX (7.7 g.) treated with 10 g. SOCl2 gave the HCl salt, which treated with K2CO3 liberated 1-chloro-3-(3-tropanyl)propane (XXXI), b1 100-2°. XXXI (5 g.) refluxed 18 hrs. with 0.1 g. NaI, 5 g. KCN, 18 ml. alc., and 8 ml. H2O gave 3-tropanebutyronitrile (XXXII), b0.3 132-5°. XXXII (3 g.) refluxed several hrs. with concentrated HCl and the product treated with 40% NaOH gave Et 3-tropanebutyrate (XXXIII), b0.5 115-19°. XXXIII (2.3 g.) similarly treated with p-tolyl magnesium bromide gave p-tolyl γ-(3-tropanyl)propyl ketone (XXXIV), b0.2 188-92°. XXXIV (1.5 g.) in 15 ml. Et2O treated with BuLi and 2-bromopyridine in Et2O gave 1-(2-pyridyl)-1-p-tolyl-3-tropanebutanol (XXXV), crystalline solid. XXXV (0.5 g.) dehydrated with 85% H2SO4, and the product reduced as described above gave 1-(2-pyridyl)-1-p-tolyl-4-(3-

tropanyl)butane. II (9.2 g.) with MeLi gave dimethyl-3-tropanecarbinol, which was dehydrated by refluxing with AcOH and concentrated HCl, and the product hydrogenated over Raney Ni to give 3-isopropyltropane as an oil. XXII (11.3 g.) treated with C6H13Li gave 1,1-dihexyl-3-(N-isopropylnortropane)ethanol (XXXVI), white solid. XXXVI (8 g.) refluxed 45 min. with AcOH and HCl gave an unsatd. product as the HCl salt which was hydrogenated over Raney Ni to 2-hexyl-1-[3-(N-isopropylnortropanyl)]octane as an oil. XXXIII (14.3 g.) similarly treated with cyclopentylmagnesium bromide gave cyclopentyl 3-(3-tropanyl)propyl ketone (XXXVII), b0.9 152-6°. XXXVII (3.5 g.) dehydrated and the product reduced over Raney Ni gave 1-cyclopentyl-1-phenyl-4-(3-tropanyl)butane, a colorless oil.

IT 119640-62-9P, 8-Butyl-3-(β-cyclohexylphenethyl)tropanium iodide
RL: PREP (Preparation)
(preparation of)

RN 119640-62-9 CAPLUS

CN 8-Butyl-3-(β-cyclohexylphenethyl)tropanium iodide (6CI) (CA INDEX NAME)

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=> FIL STNGUIDE

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 150.16 | 322.47 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -21.84 | -21.84 |

FILE 'STNGUIDE' ENTERED AT 08:48:55 ON 06 JUN 2007


FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jun 4, 2007 (20070604/UP).

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(FILE 'HOME' ENTERED AT 08:42:24 ON 06 JUN 2007)

FILE 'REGISTRY' ENTERED AT 08:42:34 ON 06 JUN 2007
L1 STRUCTURE UPLOADED
L2 4 S L1
L3 133 S L1 FULL

FILE 'CAPLUS' ENTERED AT 08:43:13 ON 06 JUN 2007
L4 28 S L3 FULL

FI[redacted]'STNGUIDE' ENTERED AT 08:48:55 ON 06 JUN 2007

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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.72 | 323.19 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | 0.00 | -21.84 |

STN INTERNATIONAL LOGOFF AT 08:56:24 ON 06 JUN 2007